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TABLE OF CONTENTS

Management of Hypertension JOHN MCMICHAEL, M.D., F.R.C.P. 933
Period of Gestation THOMAS MCKEOWN, M.D., Ph.D., and J. R. GIBSON, Ph.D., M.B. 938
Oesophagitis J. B. HARMAN, F.R.C.P. 941
Determination of Cholinesterase Activity in Human Blood W. N. ALDRIDGE, Ph.D., and D. R. DAVIES, M.SC. 945
Carcinoma of the Oesophagus R. H. FRANKLIN, M.B., F.R.C.S., and J. J. SHIPMAN, M.B., F.R.C.S. 947
Cancer of the Hypopharynx and its Surgical Treatment RONALD W. RAVEN, F.R.C.S. 951
Absolute Viability in Water of S. typhi and the Dysentery Bacilli J. F. D. SHREWSBURY, M.D., D.P.H., and G. J. BARSON, F.I.M.L.T. 954
Case of Myositis Ossificans Progressiva ROY H. MAUDSLEY, F.R.C.S. 954
Case of Glandular Fever with Cerebral Complications I. M. LIBRACH, M.B., D.P.H. 956

MEDICAL MEMORANDA
Wandering Spleen During First Decade of Life. C. L. HALL, B.M., B.Ch. 957
Trauma and Fibrosarcoma in the Foot. E. SILVERSTONE, L.R.C.P.&S.Ed. 958

REFRESHER COURSE
Heart Block. GEOFFREY BOURNE, M.D., F.R.C.P. 966

GENERAL ARTICLES AND NEWS
CANCER RESEARCH JUBILEE 968
MEDICAL NOTES IN PARLIAMENT 978
UNIVERSITIES AND COLLEGES 979
MEDICAL NEWS 982
BIRTHS, MARRIAGES, AND DEATHS 984
QUESTIONS AND COMMENTS 985

OBITUARY
Sir Milsom Rees, K.C.V.O., F.R.C.S.Ed. 975
Sir David Wallace, K.B.E., C.M.G., LL.D., F.R.C.S.Ed. 976
G. B. Fleming, M.B.E., M.D., LL.D., F.R.C.P., F.R.F.P.S. 977
R. J. Mills, M.B. 977
J. Howard-Jones, M.D., D.SC. 978

MEDICO-LEGAL
Royal College a "Charity" 979

Vital Statistics 980

LEADING ARTICLES
Surgery of the Oesophagus 961
Epidemiology of Hypertension 962

ANNOTATIONS
Growth and Development of Children 963
Acetylcholine Treatment in Psychiatry 964
Arteriotomy 965
Pneumoconiosis in Gold Mines 965

REVIEWS
The Sensitive Colon 959
Flowers and Fruits 959
Public Health Administration 959
Radiology of the Pancreas 960
French Psychiatry 960
Infant Feeding 960
Guide to Nursing 960

REPORTS OF SOCIETIES
ROYAL SOCIETY OF MEDICINE: Spread of Infection in the Family 968

SUPPLEMENT
Full Contents on First Page of Supplement
General Medical Services Committee 209
Deadlock at Durham 225
Chest Physicians 225
Dismissal from Medical Boards 225

CORRESPONDENCE
Isonicotinic Hydrazide as Wonder Drug. ANDREW MORLAND, M.D.; L. H. EUNSON, M.B. 970
Family Planning. JOAN MALLESON, M.B.; JOYCE GRANT, M.R.C.S. 970
Discharge of Certified Mental Patients. C. R. BERNIE, M.D. 971
Physiology of Sleep. NATHANIEL KLEITMAN, Ph.D. 971
Prolonged Respiratory Paralysis after Succinylcholine. REX BINNING, M.B.C.S.; C. LANGTON HEWER, M.B. 971
Mental Disease a Symptom of Physical Defect. M. J. KENNEFICK, M.B. 972
Explosion During Anaesthesia. J. F. BURDON, M.B. 972
Sponge-rubber Collar for Cervical Disk Lesions. T. T. STAMM, F.R.C.S. 972
Effect of Sulphonamides on Mortality. ROBERT HUGHES, M.D. 972
Goat's Milk and Infantile Eczema. BETHEL SOLOMONS, jun., M.D.; K. LINDENBAUM, M.R.C.S. 973
Intra-partum Uterine Rupture. C. J. DEWHURST, M.B., and H. A. ROWLEY, M.B.; D. B. SCOTT, M.B. 973
Damnable Heresy? J. VERNON BRAITHWAITE, M.D. 974
Streptomycin in the Tuberculous Knee-joint. J. A. CHOLMELEY, F.R.C.S. 974
Mr. Bevan. W. M. MAXWELL, M.B. 974
Fouling the Nest. COLIN HURRY 974

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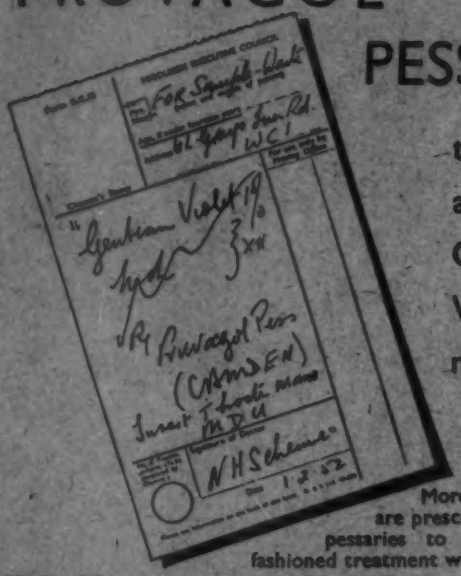

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 3 1952

THE MANAGEMENT OF HYPERTENSION*

BY

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With the conquest of infections and resulting prolongation of life, hypertension and arteriosclerosis have become the major causes of illness, disablement, and death, especially in the second half of life. The confusion and difficulty which used to arise in differentiating hypertension from chronic nephritis has largely been cleared up, and we owe a great deal of our new understanding of the relationship between these conditions to the work of Ellis (1942) and Wilson and Byrom (1939), of the London Hospital School.

Factors in Pathogenesis of Hypertension

Over a century has elapsed since Ludwig invented the kymograph in 1847, since when the regulation of arterial pressure and the related topic of distribution of blood flow have been subjected to more close and critical study than perhaps any other subject in physiology. Vasomotor centres, carotid sinus reflexes, aortic reflexes, adrenaline (now known to be secreted with *nor*adrenaline), and a host of other factors—nervous, humoral, and metabolic—have been thought, in turn, to provide possible keys to the practical mastery of blood-pressure regulation. The stupendous efforts of several generations of scientists have produced an ever-growing halo of light which merely illumines an ever-increasing sphere of darkness. Richard Bright recognized the association of nephritis and hypertension, and in the last two decades great efforts have been made to comprehend this relationship. It seems well established that a kidney with its blood flow reduced produces a substance—renin—which induces vasoconstriction (Goldblatt, 1947). Other investigators (Shorr, 1948) think, however, that renin is not the only substance concerned, and that another vasoexcitor material (V.E.M.) is formed by the ischaemic kidney. Another school believes that the kidney normally eliminates or neutralizes some pressor substance formed elsewhere in the body, as hypertension can develop in nephrectomized animals kept alive by various means (Muirhead *et al.*, 1949).

Recently a good deal of attention has been given to the possible role of the suprarenal cortex in the production of hypertension. Fisher and Hewer (1947) have shown the frequency of suprarenal cortical hyperplasia and increased cortical lipoids in patients dying of hypertension. An excess of deoxycortone acetate in the treatment of Addison's disease can induce hypertension, while a salt-free diet—for example, the rice diet—will bring the pressure down (Cameron *et al.*, 1950). In a recent lecture Professor Rosenheim (1951) emphasized the possible role of sodium in hypertension. Reports from the London Hospital show that some forms of experimental hypertension depend on the presence of intact suprarenal glands, and throw up the possibility that altered sodium balance may be important in disturbing vascular tone (Floyer, 1951; Ledingham, 1951). Attractive though this view may be, efforts to demonstrate increased excretion of suprarenal cortical substances in the urine of hypertensives have not yet succeeded.

Less tangible factors have been sought in race, heredity, and relation to obesity and the menopause. From the follow-up of pre-eclamptics it has been shown that many of these patients who have had transient hypertension in pregnancy become cases of essential hypertension some years later (Browne and Dodds, 1939). We all recognize the association between hypertension, arteriosclerosis, and diabetes, but in such patients high pressure *per se* seldom becomes severe, though the associated arteriosclerotic lesions are often severe and contribute to the final breakdown. The part played by stress, strain, and worry in the production of hypertension is very difficult to evaluate, but it is of interest to notice that Smirk (1949) and his associates claim to have produced hypertension in rats following exposure (in a sound-proof room) to the continually recurring blast of a klaxon horn.

Hypertension and Arteriosclerosis

It is generally held now that the anatomical thickening of the arteries and arterioles which is an almost universal accompaniment of the terminal stages of hypertension does not in itself produce hypertension but rather the converse: the raised pressure within the arteries leads to reactive thickening of their walls. Volhard (1948), whose contribution to the subject deserves our highest praise, had the following hypothesis of hypertension. Emotion, worry, and similar strains raise the cardiac output. This rise in cardiac output does not normally raise the blood pressure, because the arterioles dilate automatically from reflexes arising in the aorta and carotid sinuses. Volhard thought that as a result of continued stimulation these reflexes became exhausted, reflex vasodilatation failed, and so the blood pressure became high. In later stages anatomical thickening of the arterioles caused persistent resistance to arteriolar flow with permanent hypertension. Nowadays we realize that the latter part of this hypothesis is wrong. We have powerful vasodilator drugs, and, so far as I

*Based on a B.M.A. Lecture given at Bolton on January 8.

can see, there is practically no hypertension which cannot be reduced to normal levels by the use of these substances. Blood vessels right through to the very last stages of hypertension are still capable of dilatation, and anatomical thickening and narrowing therefore play little part in the production of high blood pressure. Reduction of blood pressure by various sympathetic "blocking" agents, moreover, does keep open the question of a neurogenic component in hypertension. In the early stages of hypertension there are certainly many instances in which excitement and emotion seem to be the major factors precipitating a rise in arterial pressure.

Recognition and Causal Analysis of Hypertension

Let us now leave hypothesis and turn to the practical problem of the recognition of hypertension and practical decisions with which we are faced in consequence of our diagnosis. Hypertension in an adult must be diagnosed when the diastolic pressure is over 90 mm. Hg. Systolic hypertension—for example, B.P. 180/80—may be due to causes like rigidity of the aorta, and is excluded from this discussion. It is possible that in the near future we may have to alter slightly our criteria for the auscultatory measurement of diastolic pressure, for recent work in the United States suggests that the point at which the Korotkoff sounds disappear may be more accurate than the point of muffling which has usually been accepted in the past. It is quite certain that when pressure is low in an artery the auscultatory method may be quite inaccurate, especially for the diastolic pressure. In measuring blood pressure the cuff should be applied firmly round the arm so that bulging of the bag does not occur. If the expanding bag escapes from under the cuff, or if its inflated volume is entirely used in displacing soft tissues, especially in fat arms, inaccurately high readings may sometimes be obtained. The expanding rubber bag must compress the artery before the elastic limits of the bag are reached.

Having decided that a subject is hypertensive, our next problem is to decide whether or not the condition is secondary to some cause which may possibly be amenable to direct treatment. Such causes are coarctation of the aorta, unilateral pyelonephritis and congenital hypoplastic kidney, and phaeochromocytoma; while in other instances there are recognizable pathological associations which it may, however, be impossible to treat at the moment. Such are nephritis, acute and chronic, congenital cystic kidney, and Cushing's syndrome. Sometimes one may see obese, plethoric, hypertensive young subjects with livid striae on the abdomen who might be called cases of "pseudo-Cushing's syndrome" (Davies and Clark, 1950). Professor Platt (1948) has with good reason emphasized the rarity of essential hypertension under the age of 40 and the high frequency of causal conditions in the kidney in such young hypertensive subjects.

Hypertension Due to Unilateral Renal Disease

When a unilateral kidney lesion is detected it is always worthwhile to have that kidney removed, especially in the younger age group. In my own experience I have encountered four such cases: in three, removal of the unilaterally diseased kidney led to great improvement; in one (Case 1), pressures were kept almost at normal levels for eight years.

Case 1.—A bricklayer aged 39 (in 1942) complained of headache and was found to have a blood pressure of 248/160. There was severe retinitis with papilloedema. Radiologically, multiple calculi were seen in the right kidney and uroselectan showed no evidence of excretory function. Right nephrectomy was performed on February 11, 1942, by Mr. R. T. Payne. Blood pressure fell to 100/75, and the fundal changes regressed until six weeks after the operation the disks were quite clear and only a few exudates could be seen. The heart, which had been moderately enlarged, diminished in size, and the patient has continued to be well, and working, over the last 10 years. B.P. in the first eight years after operation fluctuated between 130/90 and 160/100, but when last seen on January 3, 1952, it had risen to 175/120.

Case 2.—A 14-year-old girl was admitted on April 29, 1941, on account of blurring of vision. She had had nocturnal frequency in 1938 and was observed in Clacton Hospital as "? abdominal emergency" in 1939, since when she had severe headaches and recently vision had become blurred. B.P. 270/160. Severe papilloedema with extensive exudates, and macular star figures with much hard white exudate between the disk and the macula, were noted. Cerebrospinal fluid pressure 240 mm. Blood urea 33 mg. Pyelography showed a small shrunken left kidney. Urine contained albumin; urea clearance was 65% of normal. The left kidney was removed on January 28, 1942, by Professor Grey Turner. It was grossly shrunken, and microscopically showed chronic pyelitis and chronic pyelonephritis. There was some endarteritis obliterans in the areas of active inflammation, but no evidence of arteriolonecrosis. After the operation her B.P. subsided to 140/90, but climbed again in the post-operative weeks to 180/120. The retinitis slowly subsided in succeeding years, and in 1948 the disk margins were clear and a few peripheral pigment deposits with pigment "peppering" at the maculae were all that could be seen. B.P. on yearly visits to hospital ranged from 160/105 to 180/115. She was last seen on December 20, 1951: B.P. 180/110; feeling well; now married and working as a secretary; the left macula was practically normal, while the right macula still showed a few pigmentary patches.

Case 3.—A 17-year-old dressmaker was admitted on March 22, 1942, under Dr. Sharpey-Schafer with headache and general tiredness. She had been recognized as hypertensive for at least three years. Albuminuria was present. B.P. 220/145. The fundi, however, showed no retinitis. Intravenous pyelography showed that the left renal outline was small, and a left nephrectomy was done by Mr. R. T. Payne on March 25. Histologically the kidney showed evidence of old pyelonephritis. The B.P. settled slowly after the operation and the most recent reading was 160/105 on December 20, 1951. She is in good health and rather obese.

Case 4.—A schoolgirl aged 12 (1942) had an epileptic fit and complained of headache with mistiness of vision. On examination the B.P. was 260/180. There was papilloedema with severe retinitis. The urine contained albumin, with red cells and hyaline casts. Uroselectan showed impaired excretion from a small left kidney. The kidney was excised on December 22, 1942, by Professor Grey Turner. After the operation the B.P. fell over two months to 170/110 and the retinitis regressed. Within a year, however, the B.P. had risen to 250/160. She again began to have fits, but the papilloedema did not recur. She continued to have very severe headaches and developed progressive cardiac enlargement. She died on May 31, 1945, two and a half years after operation.

Comment.—Case 1 gave the best result, with restoration of pressure to nearly normal levels for eight years, but he is now definitely hypertensive again. Cases 2 and 3 were partial successes, with restoration of severe hypertension to more benign levels, while Case 4 showed only a short remission. Successful treatment of hypertension by nephrectomy is thus a rare event. More often one encounters bilateral kidney disease for which nothing can be done. Generally speaking, the search for causal renal disorder is worth while in hypertensives under the age of 45, but after this age renal causes amenable to treatment are highly improbable.

Essential Hypertension

Once we have decided that hypertension is not secondary to any of these causal conditions the diagnosis will be essential hypertension. There are various categories of clinical severity. In ascending order of gravity, we may list these as follows:

1. *Intermittent* hypertension. Casual readings of elevated pressure are found which subside to normal with rest and

reassurance. The rises of pressure are sometimes ascribed to nervousness and emotion. Considering the state of anxiety in which most patients must come to see a hospital consultant, we cannot ascribe these high readings to nervousness alone. A follow-up of American soldiers with occasional hypertension showed that a majority of them became more persistently hypertensive in later years (Levy *et al.*, 1944).

2. *Remittent* labile hypertension, which subsides to a lower but not quite normal level with rest in bed and with sleep, but which remains benign and often symptom-free for many years.

3. Hypertension which is *sustained* although it continues to show some fluctuations. (*a*) This sustained hypertension may be *uncomplicated* for many years. (*b*) Sooner or later important organs become involved—brain, eye, heart—and it is a matter of chance which of these is involved first. Severe and disabling headaches should be included among the meningo-vascular cerebral complications. This stage can be called *sustained complicated* hypertension.

4. Hypertension with severe active retinal involvement but without papilloedema. In such cases there is usually evidence of cardiac strain and/or cerebral vascular complications: the diastolic pressure has by then risen to above 120 mm. Hg, and in this group the course is usually rapid, terminating in two to three years. This is often called the *pre-malignant* phase.

5. *Malignant* hypertension with retinitis and papilloedema (hypertensive neuroretinopathy). In this condition rapid cerebral, cardiac, and *renal* involvement takes place and patients nearly always die within a year.

Assessment of Prognosis

The course of the disease is usually benign for many years, especially in the first two of the above groups. In the third group the course is also benign for long periods, until visceral complications alter the outlook. In the fourth and fifth groups the eye grounds are a remarkably useful guide to prognosis. The more severe and active (fresh haemorrhages and soft cotton-wool exudates) the retinitis the worse the outlook, and in the presence of oedema of the optic disk patients seldom survive more than a few months. The prognostic value of eye-ground changes was clearly demonstrated by Keith, Wagener, and Barker (1939) (see Table).

Fundus Changes in Hypertension and Corresponding Prognosis (From Keith, Wagener, and Barker, 1939)

Grade	Fundus Oculi	Prognosis
1	Only mild narrowing or sclerosis of retinal arterioles	70% alive after 7 years
2	Moderate to marked sclerosis of retinal arterioles. May be some hard white patches	50% „ „ 5 „
3	Cotton-wool exudate, haemorrhages, and oedema of retina superadded to above	75% dead in 3 years
4	As in grade 3, but with oedema of the optic disks	90% „ „ 1½ „

In so far as higher diastolic pressures are associated with retinal lesions of increasing severity and greater chances of cardiac strain, the prognosis becomes worse, and the condition will always cause anxiety when the diastolic pressure has exceeded 120 mm. Hg.

There are, however, many exceptions to all these rules. When the blood pressure has risen *very slowly* over a long period of years quite high pressures may be well tolerated, and women seem to stand them much better than men. Particularly after the age of 60, very high pressures may be encountered with a good prognosis and little retinitis (Burgess, 1948). This contrasts with *rapid* rises of pressure to high levels in primary malignant hypertension with consequential arteriolar necrosis. Blood and Perera (1948) have reported a series of 50 patients who survived ten years or more: in 21 of these there were high diastolic pressures reaching 120 mm. Hg or over and even retinitis at the beginning of this long survival period. On rare occasions even malignant hypertensive neuroretinopathy may regress spontaneously. I have seen this happen only twice in the last 12 years, with the unexpected survival of the patients for two and three years respectively.

Treatment

In the symptom-complex of hypertension there is enough evidence that the hypertension itself is harmful, and that anatomical changes in the arteries on which thrombosis may occur are a long-term consequence of the elevated pressure. Reduction of pressure is therefore desirable. It should be remembered, however, that there are two vascular areas in which blood flow is mainly dependent on the level of the aortic pressure. These are the coronary and cerebral vascular beds. Reduction of blood pressure will almost certainly reduce blood flow in these situations, and in the presence of atheromatous changes in the coronary and cerebral vessels a reduced rate of flow may favour local thrombosis. Blood-pressure reduction should therefore not be lightly undertaken in patients who have shown any gross evidence of cerebral and coronary vascular occlusion.

The measures available for reduction of blood pressure are at present somewhat unsatisfactory, because we know of nothing that will neutralize the causal agencies, which still remain unknown in hypertension. Our remedies are complicated in use and only partially successful, the effects are difficult to maintain over long periods, and there are often unpleasant side-effects or even risks of harm from their indiscriminate application. The approach which I shall outline is purely a personal one, from which no doubt other experienced physicians would differ.

In our present state of knowledge we do not attempt drastic blood-pressure reduction in the benign uncomplicated hypertensives of the first three groups outlined above. Often the diagnosis need not be revealed: otherwise great personal skill and a persuasive authoritative manner may be required to reassure the patient that his hypertension is a benign condition, and likely to remain so for many years. We must not complicate a benign and often practically symptomless condition by an anxiety neurosis. Mild sedation with phenobarbitone or "theominal" may be helpful, especially in tense subjects, and weight reduction should be prescribed in the obese.

As already emphasized, patients with extensive thrombotic, cerebral, or coronary lesions should also be handled with care, as blood-pressure reduction may be risky. In elderly subjects who have had hypertension for many years, complicating vascular anatomical change may be assumed to be present, with the attendant possibility of thrombosis when pressure is reduced. Systematic efforts at pressure reduction are therefore limited to pre-malignant and malignant hypertension (groups 4 and 5 of our suggested classification) and where complications are present or impending in patients with sustained hypertension (group 3*b*).

Methods of Blood-pressure Reduction: 1. Sympathectomy

Extensive removal of the sympathetic chain from the mid-thoracic or lower thoracic region to the upper lumbar ganglia on both sides has had its vogue. Putting together the cases reported in this country by Chris (1951) (33 cases), Platt and Stanbury (1950) (80 cases), and Northfield (1948) (29 cases), significant reduction of blood pressure was apparently achieved in 26 out of the total 142 cases, or 18%. For the most part these were early results judged within two years or so of the operation. A most careful study by Evelyn and his associates (1949) showed that early reduction of blood pressure after sympathectomy was not sustained and that at the end of five years only 21% of the patients operated on had any significant reduction of arterial pressure. Practically 80% of the operations therefore give poor results so far as blood-pressure reduction is concerned. Furthermore, the operation has a mortality, and it is certainly not

a universal treatment for hypertension. These disappointing results may find a partial explanation in certain recent investigations.

Boyd and Monro (1949) have shown the existence of "intermediate" sympathetic ganglia outside the sympathetic chain, making *total* sympathectomy impossible even regionally. Furthermore, Barcroft and Hamilton (1948), in a complete study of sympathectomized upper limbs, have shown recovery of tone and reactivity in the small vessels after a few months, and the work of Wilkins *et al.* (1949) suggests that similar recovery takes place in the splanchnic area. Evelyn and his colleagues (1949) have noted good results (B.P. down to normal or nearly normal) in only 8% of operated cases.

If we could only select with certainty those few cases which do respond we should be very pleased to continue recommending sympathectomy, but unfortunately all the preoperative tests to improve selection which have been tried seem to have failed utterly. We must reluctantly admit that a large number of quite useless operations have been performed and that there is very little prospect of any satisfactory improvement in surgical technique or selection in the near future.

2. Adrenalectomy

Total extirpation of the suprarenals has been tried (Green *et al.*, 1950), with maintenance of life by subsequent administration of suprarenal cortical hormones. More information on the long-term results is needed before we can pass judgment.

3. Medical Measures

(*a*) *Salt Depletion.*—Restriction of sodium intake will often bring down the blood pressure, and this is the basis of Kempner's (1948) rice diet. The diet consists of rice, fruit juices, and sugar, supplemented by vitamins and iron. It contains a low protein content of 20 g. a day, and the daily sodium intake is 200 mg. It is generally agreed now that the blood-pressure reduction achieved on this diet is due to sodium depletion, and any other kind of diet in which the daily sodium content is down to 200 mg. or less would be equally effective (Cameron *et al.*, 1950). Patients usually are unable to continue taking tasteless and insipid food over long periods. Recently, ion exchange resins, which prevent the absorption of sodium from the gut, have been used to permit the ingestion of a palatable diet, but there are still considerable practical difficulties about their administration (Page, 1951). Salt depletion, if pushed too far, may be dangerous by inducing uraemia, and this is particularly to be remembered in the malignant and pre-malignant phases of hypertension.

(*b*) *Thiocyanates* have had some vogue in the treatment of hypertension. They have a narrow margin of safety, blood levels have to be controlled at 8–12 mg./100 ml., and there are various unpleasant side-effects. They are said to relieve headaches, though in most cases the blood pressure does not fall. Page (1951) reports the use of sodium nitroprusside (30 mg. four times a day in capsules), which is probably converted into thiocyanate in the body. If these substances are used biochemical control of the blood thiocyanate level is necessary, and this makes them laborious and difficult to use with any prospect of satisfaction.

(*c*) *Soluble bacterial pyrogens* ("pyromen") have been used by Page and Taylor (1949). They are infused continuously to give a temperature of 101 to 102° F. (38.3 to 38.9° C.) each day. These pyrogens have been shown to dilate the kidney blood vessels, and a few successes have been achieved in cases of malignant hypertension. Reporting on this, Page (1951) said: "This is a harsh treatment, but malignant hypertension is more than harsh; it is lethal."

(*d*) *Veratrum Alkaloids.*—"Veratrone," "vertavis," and veratridine have been used to reduce the blood pressure. They have long had a place in the treatment of acute blood-pressure rises in eclampsia. They act by inducing a reflex vasodilatation, the afferent fibres of the reflex arc arising in the coronary vascular bed. With Dr. M. E. Etheridge, of Melbourne, we have tried these preparations, but the margin between an effective dose and one which induces vomiting, sweating, and other unpleasant side-effects was too small. One patient took his dose about 6 a.m. in order to get the vomiting over before breakfast at 7.30. Even this enthusiast failed to achieve any real benefit from the drug, and finally gave it up. Kauntze and Trounce (1951), using "veriloid" (veratrum viride), think that useful results may be achieved in about 20% of cases; Page (1951) puts the percentage at 15. The hopes raised by an early report of Freis and Stanton (1948) have not been confirmed.

(*e*) *Dihydrogenated alkaloids of ergot* have been used in hypertension. These substances have a sympathicolytic action. Dihydroergocornine is one of these substances which lower blood pressure and reduce heart rate. Not all hypertensive patients respond to its administration, and the reductions of diastolic pressure which are achieved are modest—10–20 mm. Hg at most (Wilkins *et al.*, 1949). "Hydergine," a mixture of three alkaloids of ergot, has also been tried with some symptomatic benefit, but again the pressure reductions are quite small. These drugs can be given orally in solution (Gibbs, 1952).

(*f*) *Hexamethonium and related compounds* were introduced into medicine mainly by the work of Paton and Zaimis (1949) at the National Institute for Medical Research. They showed that pentamethonium and hexamethonium compounds suppressed transmission in autonomic ganglia. The therapeutic possibilities of these compounds in hypertension were realized almost simultaneously by Restall and Smirk (1950) in New Zealand and by Turner (1950) in Edinburgh. Controversial claims have followed, some writers condemning the drug as valueless—for example, Locket *et al.* (1951)—and others, particularly Smirk, claiming excellent and striking results. There is not the slightest doubt that the drug is difficult to use, and when continued in effective doses will quite often be accompanied by very unpleasant side-effects. The same could of course be said of the indiscriminate use of digitalis, and we must not overlook valuable therapeutic possibilities because of difficulties in selection of cases and because of problems created by individual dosage regulation. The dosage required to produce effects is very variable in different individuals, and a certain amount of tolerance usually develops, which requires a great deal of patience to overcome.

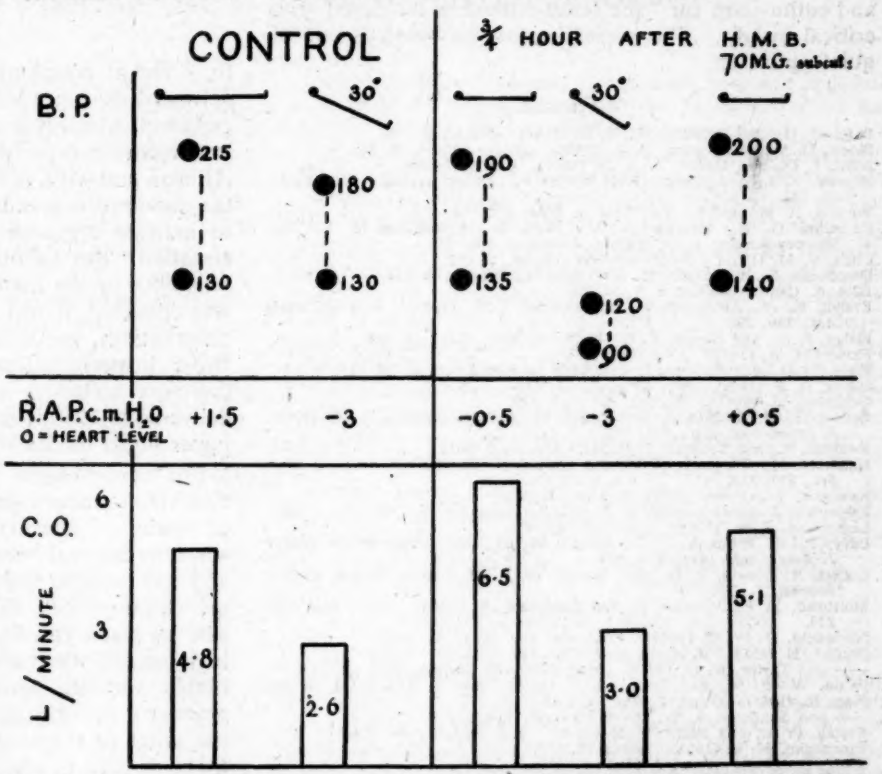
Absorption of the orally administered drug is irregular and difficult to control (Kilpatrick and Smirk, 1952). It is difficult to obtain satisfactory therapeutic results by this route, and local gastro-intestinal troubles, like vomiting and paralytic ileus, seem to be more likely to occur when the drug is given by mouth. For this reason we have adopted the subcutaneous injection method recommended by Smirk and Alstad (1951), the patients treating themselves like diabetics with their injections of insulin. We have restricted our choice of patients for treatment to severe and complicated cases (groups 3*b*, 4, and 5).

Our results have been as follows. In all, 27 cases have been treated by subcutaneous injection. A single effective dose will bring pressures well down towards normal levels for two to three hours, after which they will climb slowly towards the control level in about six to eight hours. The malignant and pre-malignant groups have totalled seven, of whom four have undergone dramatic improvement, while three, who were in a very advanced stage when treatment was begun, died of uraemia, cerebral haemorrhage, and heart failure. (Two of the three who died showed temporary improvement of vision and regression of their retinopathy before their final deterioration.) In the others we have not only had visual improvement, objective and subjective, but disappearance of headaches and restoration of working capacity, diminution of heart size, and regression of electrocardiographic changes, which are very gratifying.

In patients with sustained hypertension with complications, good reductions of pressure are being achieved by twice- or

thrice-daily injections, and in those able to continue treatment headaches are controlled and working capacity is restored. Five patients out of 27 have been unable to continue to co-operate on account of severe side-effects or inability to carry out a rather exacting regime. (These results will shortly be communicated in more detail by Dr. Brenda Morrison.) One great advantage of the subcutaneous route is that untoward side-effects like meteorism, sickness, diarrhoea, etc., subside in a matter of hours on omission of one or two doses. We have not yet failed to reduce blood pressure, though dosage has had to reach high levels, as high as 750 mg. subcutaneously in one subject, given as 2.5 ml. of 30% solution deeply under the skin with a little procaine to avoid the pain which would otherwise result from such a hypertonic solution.

The greatest reduction of blood pressure is achieved by taking advantage of the postural drop, as recommended by Smirk and Alstad (1951). When a normal individual stands up or is quickly turned to a feet-down slope while relaxed on a comfortable couch his cardiac output falls by about 30 to 40% owing to pooling of blood in the lower half of the body. The blood pressure does not fall, however, because of reflex vasoconstriction. Under the influence of hexamethonium, this reflex is blocked and the blood pressure drops in parallel with the cardiac output (see Chart). It is an excellent thing, therefore, to keep patients on hexamethonium treatment on their feet as much as possible and doing their work. When resting, they should sit in a high chair in order to take as much advantage as possible of gravity effects on the circulation. Treatment in bed is much less effective. Even patients with malignant hypertension are encouraged to be up out of bed or sitting in a high chair for the greater part of the day. With the use of these measures treatment has usually been satisfactory.



The effect of posture on blood pressure in a hypertensive subject before and after hexamethonium bromide. Before administration of the drug a fall in cardiac output induced by tilting feet down is compensated by vasoconstriction, and the diastolic pressure remains unchanged. A similar fall in cardiac output takes place under the influence of hexamethonium, but the reflex inducing vasoconstriction is blocked—pressure falling in proportion to the cardiac output.

The presence of some degree of nephritis with a raised blood urea is no contraindication to treatment. Young and others (1951) have shown that the excretion of hexamethonium into the urine parallels the glomerular filtration. The amount of fluid filtered at the glomeruli is low in nephritis, and therefore we would expect the effect of a single injection to last longer in nephritic subjects. This, in fact, seems to be the case. Nephritics with a moderate degree of kidney impairment respond, for a time at least, particularly well to hexamethonium. We have noticed no special tendency for the blood urea to rise while on treatment. Various vasodilatory influences or other measures which tend to reduce blood pressure seem to enhance the effect of hexamethonium. Among these we may list the taking of a meal (which presumably dilates the splanchnic vascular bed), restriction of salt intake, and intercurrent febrile illnesses. Perhaps the addition of some other mild vasodilatory drug to hexamethonium may in future be found to be better than hexamethonium alone.

(*g*) *1-hydrazino-phthalazine.*—Page (1951) has reported recently that this drug has a moderate influence in reducing the diastolic pressures, possibly through some central action. It has apparently no effect on the blood pressure in the spinal animal, which suggests that its action lies in the vasomotor centres higher up in the nervous system. It may be given by mouth in doses of 25 to 75 mg. Tolerance, however, quickly develops, and some unpleasant actions, like flushing of the face, palpitations, sweating, and a feeling of breathlessness, have been noted. Page (1951) reports that 33 of 70 patients had a fall of diastolic pressure of 20 mm. Hg or more while on the drug. The average total daily dose used varied from 100 mg. to 1.4 g. Good responses were reported to occur eventually in patients who had no lowering of pressure in the first ten days of treatment.

So far, we have tried this substance on only a very small number of patients, and we only recently became aware of the suggestion that effects might not occur until one to two weeks had elapsed. The drug may well be worthy of further trial along these lines.

Conclusion

I have written enough to indicate that we have passed the stage when we were powerless to help the severe hypertensive except by taking a chance on surgical sympathectomy. Drugs of possible use are now reaching us in abundance, almost beyond our capacity for reasonable trial. Streptomycin won its place in the therapy of tuberculosis by its success in tuberculous meningitis, otherwise universally fatal. Drugs which have a place in hypertension will first prove themselves in the most severe forms, malignant and pre-malignant. Thereafter their influence on the more chronic and less severe cases will be shown only by prolonged and carefully planned statistical trials. We should not rush too soon to a combination of remedies, but rather study and record the effects of individual drugs so that we may know exactly what we are doing. Effective hypotensive agents are complicated in use, and should be reserved

for cases judged to have a bad prognosis. If a very high and sustained pressure is made to fluctuate at a lower level the whole course of the illness may possibly be more benign. Too great a reduction of pressure may be associated with some risks, especially in those who have had raised pressures for years. The powerful remedies now at our disposal must be used with caution, and their effects, good and ill, must be carefully documented. The desire to find benefit for our patients and enthusiasm for "the latest" must be tempered with critical insight. The present mood, however, is one of quiet optimism.

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The tenth session of the W.H.O. Expert Committee on the International Pharmacopoeia met on April 23–30 in Geneva. For the tenth time Dr. C. H. Hampshire, of London, was elected chairman of the committee as a tribute to his outstanding contribution to the recently published *International Pharmacopoeia* (Vol. I). In the course of this session the Expert Committee have completed the preparation of Vol. II of the *International Pharmacopoeia*, which will include about 200 monographs, many of them describing new drugs, injections, etc., as well as a dozen important appendices indicating biological assays, tables of doses for children, and tables of usual and maximal doses for adults. When completed, this volume will be published simultaneously in English and French. A Spanish edition is to follow soon thereafter. This will complete the first edition of the *Pharmacopoeia*, which will be extended and kept up to date by an *Addendum* to be issued the following year, and a second edition in 1955, again in English, French, and Spanish. A meeting of the Subcommittee on Non-proprietary Names followed on May 1 and 2. This selects internationally approved non-proprietary names for drugs, to prevent the confusion which arises from the use in different countries of different names for the same drugs. So far 600 international names for drugs have been selected, and the subcommittee is to consider 200 other new names.

THE PERIOD OF GESTATION

BY

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In a recent communication 17,145 Birmingham births delivered during 1947 were distributed by duration of gestation, which was estimated from the first day of the last menstrual period preceding pregnancy to birth (Gibson and McKeown, 1950). We were asked whether the distribution could be used for medico-legal purposes to indicate the probable upper limit of the period of gestation. But although we had no reason to doubt the reliability of the material for the purposes for which it was collected, it was not possible to rely on individual observations, particularly in the later weeks, without a closer inspection than was then provided. We have therefore collected information on Birmingham births delivered in 1950 in order to examine more carefully the upper limits of the period of gestation.

For medico-legal purposes it would of course be desirable to record the period of gestation from the date of coitus or, alternatively, from the date of ovulation, since the interval between coitus and ovulation is shorter and less variable than between coitus and the preceding menstrual period. But in practice neither of these dates can be given for the large series of births needed (at least several thousands) to establish the range of the highly variable period of gestation. It is therefore necessary to estimate the period of amenorrhoea from the onset of the menstrual period preceding pregnancy to birth, and to make an adjustment for the probable interval between the onset of the menstrual period and coitus.

The Period of Amenorrhoea

The period of amenorrhoea was recorded in this way from health visitors' cards for 15,659 of the 18,819 births delivered in Birmingham during 1950. (Birmingham health visitors obtain the date of onset of the last menstrual period from antenatal documents and are asked to record the date only if it is definite.) The distribution is given in Table I. As we are here interested only in the longer intervals, births delivered before the 41st week are grouped. There were 247 births after the end of the 44th week, of which seven were born later than 48 weeks. The two longest periods were 356 and 359 days.

We cannot, of course, accept these estimates as reliable without consideration of certain obvious sources of error.

(*a*) *Uncertainty Regarding which Bleeding has been Followed by Coitus and Fertilization.*—Bleeding in the early months of pregnancy is not uncommon and may be confused with the preceding cycle. Thus the estimate may be too short if dated from bleeding during pregnancy, or too long if dated from the penultimate cycle, the last cycle being mistaken for post-ovulatory bleeding. These difficulties could of course be overcome by use of pregnancy diagnosis tests at the appropriate time (after the first missed cycle and before further bleeding), but such tests are not at present in general use.

(*b*) *Misleading Information from the Mother.*—It is well known that premarital conception, particularly of first births, is not uncommon, and provides the mother with a motive for post-dating the last menstrual cycle. Alternatively, in

TABLE I.—*Cases Delivered in Birmingham in 1950 Distributed According to the Period of Amenorrhoea (from Onset of the Last Menstrual Period to Birth)*

Delivered in	Week:	Under 41	41	42	43	44	45	46	47	48	49	50	51	52	All Births for which Date of L.M.P. was Recorded	All Births for which Date of L.M.P. was Not Recorded	All 1950 Births
	Days:	280 and under	281–	288–	295–	302–	309–	316–	323–	330–	337–	344–	351–	358–364			
No. of births ..		5,342	4,947	3,220	1,406	497	144	62	23	11	5	—	1 (356 days)	1 (359 days)	15,659	3,160	18,819
%		34·12	31·59	20·56	8·98	3·17	0·92	0·39	0·15	0·07	0·03	—	0·01		100	—	—

cases of medico-legal interest, the mother may antedate the period in order to establish the identity of the father. In the first case the effect is to reduce the estimated period of amenorrhoea, and in the second case the effect is to prolong it.

(*c*) *Indefinite or Inaccurate Dates.*—Not infrequently only an approximate date can be given for the first day of the last menstrual period, or, with no intention to mislead, and in absence of any confusion about the relevant cycle, the mother may give a wrong date. Errors may also occur subsequently during transcription of the data to other documents or punch cards.

In the present context we are concerned only with errors which might increase the estimate of the period of amenorrhoea. These arise, first, from uncertainty regarding which bleeding has been followed by fertilization, and, secondly, from indefinite or inaccurate dates. Misleading information which would lengthen the period of amenorrhoea is only likely in the exceptional case coming to the courts.

TABLE II.—*Cases Delivered After the End of the 44th Week in Which the Estimated Period of Amenorrhoea was Considered Reliable*

Delivery in		Original No. of Births	No. of Births for which Period of Amenorrhoea was Considered Unreliable				No. of Births in which Period of Amenorrhoea was Considered Reliable
Week	Days		Mother not Interviewed	Date of L.M.P. Unreliable	Bleeding in Early Months of Pregnancy	Total	
45	309–315	144	10	46	12	68	76
46	316–322	62	10	23	3	36	26
47	323–329	23	—	17	2	19	4
48	330–336	11	—	8	1	9	2
49	337–343	5	—	3	1	4	1 (339 days)
50	344–350	—	—	—	—	—	—
51	351–357	1	—	1	—	1	—
52	358–364	1	—	—	—	—	1 (359 days)
Totals		247	20	98	19	137	110

As a check on the reliability of information recorded for the 247 births delivered after the 44th week, all relevant antenatal documents were examined and the mothers were interviewed at home. Data recorded from the mother included details of all previous pregnancies and for the pregnancy under consideration; menstrual history in the preceding six months; history of bleeding in the early months; and date of onset of the last menstrual period. In respect of the last question mothers were asked if they remembered or had a record of the date of the period or of the expected date of delivery, and, if not, whether the date given at the first antenatal examination was definite. Cases were then accepted as reliable only if (*a*) the date of onset of the last menstrual period was recorded unequivocally on the antenatal record and confirmed by the mother, and (*b*) there was no history of bleeding in the early months of pregnancy. Table II shows that of the 247 births, 137 were excluded—20 because the mother was not interviewed, 98 because the date of the last menstrual period was considered unreliable, and 19 because there was a history of bleeding in the early months of pregnancy. We are left with 110 births delivered after the end of the 44th week, in respect of which the period of amenorrhoea was thought reliable.

Table III gives details of the seven cases in which the period of amenorrhoea was originally given (in Table I) as longer than 48 weeks (336 days). On the criteria here used only two of them can be accepted (339 and 359 days).

The Period between Coitus and Birth

For medico-legal purposes the period of interest is that between coitus and birth. This can be obtained by adjusting our estimates of the period of amenorrhoea according to the probable minimum interval between the onset of the last menstrual period and coitus. If the menstrual cycle is regular and of approximately 28 days, a moderately accurate assessment of this interval can be made; but if the cycle is irregular or prolonged, considerable error may be introduced because of variation in the time between the onset of menstruation and the ovulation which follows. It has therefore been considered necessary to exclude all cases in which the mother stated that her menstrual cycle was irregular in the six months before pregnancy began (see Table IV). Of the 110 births delivered after the end of the 44th week in which the period of amenorrhoea was considered reliable, a further 35 are now eliminated for this reason. We are left with 75 births in respect of which the period of amenorrhoea was more than 44 weeks; three were born in the 47th week (324, 325, and 326 days) and two in the 48th (330 and 333 days). Table V gives further details of these five pregnancies, which we regard as the longest in which we can with fair confidence both (*a*) accept the period of amenor-

TABLE III.—*Details of 7 Cases in Which the Period of Amenorrhoea was Stated to be 336 Days (48 Weeks) or Longer*

	Period of Amenorrhoea (Days)						
	336	338	339	339	342	356	359
Menstrual cycle: Regularity ..	Irregular (1–2 months)	Regular (35 days)	Irregular (6–10 weeks)	Regular (28 days)	Data	Irregular	Irregular (1–3 months)
Flow (days) ..	4–5	3–4	7	7	not	Irregular	3–6
Date of L.M.P. ..	Indefinite	Definite	Definite	Indefinite	available	Indefinite	Definite
Bleeding in early pregnancy	None	Slight show at 2 months	None	Slight bleeding at beginning		None	None
Maternal age ..	24	17	29	23	24	22	38
Birth rank of child	1	1	2	2	2	2	8
Onset of labour ..	Spontaneous	Spontaneous	Surgical induction	Spontaneous	Spontaneous	Spontaneous	Caesarean section
Birth weight ..	7 lb. 4 oz. (3·3 kg.)	8 lb. 8 oz. (4 kg.)	7 lb. 12 oz. (3·5 kg.)	6 lb. 2 oz. (2·8 kg.)	7 lb. 9 oz. (3·4 kg.)	8 lb. 8 oz. (4 kg.)	10 lb. (4·5 kg.)
Sex of child ..	Male	Female	Male	Female	Male	Male	Male
Condition of child*	Live-born	Live-born	Live-born; no evidence of post-maturity	Live-born; normal	Live-born; normal	Live-born; normal	Live-born; no evidence of post-maturity

* Condition is given as recorded in delivery notes. In only two cases was there a specific reference to maturity.

TABLE IV.—*Cases Delivered After the End of the 44th Week of Amenorrhoea in Which (a) the Period of Amenorrhoea was Considered Reliable and (b) Regular Menstrual Cycles Preceded Pregnancy*

Delivery in		No. of Births in which		
Week	Days	Period of Amenorrhoea was Considered Reliable	Irregular Menstrual Cycles Preceded Pregnancy	Regular Menstrual Cycles Preceded Pregnancy
45	309–315	76	22	54
46	316–322	26	10	16
47	323–329	4	1	3
48	330–336	2	—	2
49	337–343	1	1	—
50	344–350	—	—	—
51	351–357	—	—	—
52	358–364	1	1	—
	Totals	110	35	75

TABLE V.—*Details of Five Cases Delivered After the End of the 46th Week of Amenorrhoea in Which (a) the Period of Amenorrhoea was Considered Reliable and (b) Regular Menstrual Cycles Preceded Pregnancy*

	Period of Amenorrhoea (Days)				
	324	325	326	330	333
Menstrual cycle: Interval (days)	28	28	28	28	30–1
Flow (days)	3	4	3	5–6	5
Bleeding in early pregnancy	None	None	None	None	None
Maternal age	23	26	21	27	19
Birth rank of child	4	6	1	1	2
Onset of labour	Surgical induction	Spontaneous	Spontaneous	Spontaneous	Spontaneous
Birth weight	5 lb. 15 oz. (2·7 kg.)	7 lb. (3·2 kg.)	7 lb. 6 oz. (3·3 kg.)	6 lb. 8 oz. (2·9 kg.)	8 lb. (3·6 kg.)
Sex of child	Female	Male	Female	Female	Male
Condition of child*	Live-born; normal	Live-born	Live-born; normal	Live-born; normal	Live-born

* Condition is given as recorded in delivery notes. In no case was there a specific reference to maturity.

rhoea as reasonably reliable, and (*b*) adjust the period of amenorrhoea to give an estimate of the period between coitus and birth.

The interval between the onset of menstruation and coitus which may result in pregnancy is determined (*a*) by the time of ovulation, and (*b*) by the period before and after ovulation during which intercourse may lead to fertilization. Most endocrinologists are agreed that ovulation occurs at about the middle of a regular 28-day cycle (Allen *et al.*, 1930; Knaus, 1934; Shaw, 1934; Latz and Reiner, 1942; Rock and Hertig, 1944), and that intercourse is likely to be fertile only within a few days of that time (for it is thought that spermatozoa are viable for at most a few days after coitus, and that ova must be fertilized within a few hours of ovulation). It would therefore be consistent with these views if we regarded 10 days as the probable minimum interval between the onset of menstruation and coitus which may result in pregnancy. But experience of artificial insemination has shown that some women become pregnant only when inseminated within a few days of the beginning of the cycle (Seymour, 1939), and, while such cases are probably explained by cycles of short duration, we cannot exclude the possibility that fertilization occasionally follows coitus earlier than the 10th day in a 28-day cycle. We shall therefore take five days as the probable minimum interval between the onset of menstruation and intercourse which may result in pregnancy. It should be said at once that our only justification for accepting this figure is that we are anxious to use the most conservative—that is, the shortest—estimate of the interval, and it would probably be generally agreed that pregnancy is most unlikely to follow intercourse earlier than the fifth day of a regular 28-day cycle.

Estimates of the period between coitus and birth can now be obtained by subtracting five days from the period of amenorrhoea given in Table IV for each of the 75 cases considered suitable for the examination. The longest estimates for the period of gestation (coitus to birth) which can be accepted with fair confidence are thus 319, 320, 321, 325, and 328 days.

Analysis of the Longest Cases of Gestation

But for legal purposes it is also necessary to inquire whether still longer periods of gestation are possible. This question is difficult to answer, but can be considered after more detailed examination of the two longest periods of amenorrhoea accepted as reliable (339 and 359 days). Both these cases were excluded from Table IV.

Case 1.—339 days. The mother was referred from the fertility clinic when 16 weeks pregnant. At 291 days the membranes were thought to have ruptured and she was admitted for medical induction, which was unsuccessful. She was readmitted at 312 days for a further medical induction, which was also unsuccessful, and again at 334 days, when oestrogen was injected. At 339 days labour was brought on by surgical induction. Labour and puerperium were normal. The child was a live-born male, weighed 7 lb. 12 oz. (3.5 kg.), and showed no evidence of post-maturity. The mother had had one previous pregnancy, which resulted in a live-born child delivered spontaneously at 294 days. She has since had another live-born child, which weighed 8 lb. (3.6 kg.) at birth, and was delivered spontaneously at 310 days.

Case 2.—359 days. The mother was seen at hospital at 329 days because delivery was thought to be overdue; the foetus was quite small, and she was asked to return in three to four weeks. At 358 days she was admitted because of obstructed labour (for which no cause was given), and the child was delivered by lower segment caesarean section. The infant was a live-born male, weighed 10 lb. (4.5 kg.), and showed no evidence of post-maturity. The mother had had seven previous live births, of which six were delivered spontaneously and one after surgical induction. Because of menstrual irregularities the period of gestation cannot be given in these cases, but all deliveries are believed by the mother to have been about two to three weeks late.

These two deliveries were conducted by senior obstetricians of the Birmingham Maternity Hospital, and we have therefore no reason to doubt the accuracy of the observations. But the period between coitus and birth cannot be estimated reliably in either case, because menstrual cycles were irregular in the six months before pregnancy began (see Table III), and hence the probable interval between onset of menstruation and coitus cannot be assessed. On the assumption previously made (that the probable minimum interval between onset of menstruation and coitus is five days) the periods of gestation (coitus to birth) would be 334 and 354 days. But in the six months before pregnancy began menstrual cycles occurred at intervals of six to ten weeks in one case and one to three months in the other, and it is very much more likely that the intervals between onset of menstruation and coitus were 28–56 and 14–77 days respectively. The corresponding periods of gestation are 311–283 days and 345–282 days.

Even if we accept 354 days as the longest period of gestation, there was only one such case among 15,659 births. We conclude that on this evidence a period of gestation (coitus to birth) as long as 354 days cannot be said to be impossible.

Discussion

It has not been the purpose of this communication to assess the present medico-legal interpretation of the period of gestation, but a few words on that subject may not be out of place. The law has for its end not justice but peace, and judicial practice in this as in other matters is to accept the last agreed ruling, and inquire whether it seems reasonable to go beyond it. On this principle there is no limit to the acceptable period of gestation, which, unlike most natural phenomena, can go up but not down.

Nevertheless it must be admitted that medical evidence has been of little assistance to the courts, for the obvious reasons that no reliable large-scale data have been available, and the experience of any single witness can provide no clear evidence. For no obstetrician, however active, can expect to see many very long periods of gestation during his working life, and those which he does see provide no basis for assessment of their frequency. In these circumstances it is not surprising that judges have preferred to rely on their own interpretation of common opinion.

The position of a medical witness consulted on this question is on all fours with that of a demographer invited to express an opinion about the longest possible duration of life. He can give a period of gestation which would generally be accepted as impossible, by quoting a figure well outside his own and everyone else's experience. He can give the longest period of gestation for which he has reasonably reliable evidence, whether from his own experience or from the medical literature, and may even be able to state the frequency with which it has been observed in a population of births. What he cannot do, and cannot be expected to do, however full the information at his disposal, is to state a precise figure below which a period of gestation is possible, and above which it is impossible. The translation of medical probabilities into legal certainties is a matter for the courts.

In attempting to provide evidence which may assist the courts we have recorded the period of amenorrhoea from onset of menstruation to birth, and have estimated the period from coitus to birth by allowing for the probable minimum interval between onset of menstruation and coitus. This is the only procedure which lends itself to investigation of the large series of births needed to establish the range of the period of gestation, since dates of coitus, ovulation, and fertilization are usually unknown. Recent legal discussion of the possible interval between coitus and fertilization is indeed irrelevant, for this interval would be of interest only if medical evidence could establish accurately the range of the period between fertilization and birth. In fact, medical evidence is no more reliable on this point than on the period between coitus and birth.

Without recapitulation of reservations expressed earlier we may summarize experience of these 15,669 births as follows: the longest period of gestation which could be accepted with fair confidence is 328 days; the longest period which could not be regarded as impossible is 354 days.

Summary

The period of amenorrhoea from onset of the last menstrual period before pregnancy to birth was estimated for 15,659 of the 18,819 Birmingham births delivered in 1950. In 247 cases the period was longer than 44 weeks (308 days) and in 7 cases longer than 48 weeks (336 days). The two longest periods were 356 and 359 days.

Of the 247 births in which the period of amenorrhoea was longer than 44 weeks, 137 were subsequently excluded, either because the date of the last menstrual period was considered unreliable or because there was a history of bleeding in the early months of pregnancy. Of the 110 periods considered reliable the two longest were 339 and 359 days.

The period between coitus and birth was assessed by subtracting from the estimated period of amenorrhoea the probable minimum interval between the onset of the last menstrual period and coitus. Before making this adjustment it was considered necessary to exclude 35 cases (of the 110 judged reliable) in which the interval between menstruation and coitus could not be assessed accurately because the mother stated that her menstrual cycle was irregular or prolonged in the six months before pregnancy began.

For the remaining 75 cases in which (*a*) the estimate of the period of amenorrhoea was reliable and more than 44 weeks, and (*b*) regular cycles of approximately 28 days preceded pregnancy, the minimum interval between onset of menstruation and coitus which might result in fertilization was taken as five days. The longest estimates of the period of gestation (coitus to birth) which could be accepted with fair confidence were then 319, 320, 321, 325, and 328 days. The possibility of periods of gestation longer than these is discussed.

We are much indebted to Dr. Enid Charles for making available to us the distribution of Birmingham births in 1950, and to Mrs. M. Hopper, who interviewed mothers whose period of amenorrhoea was longer than 44 weeks. We are also grateful to the staffs of Birmingham hospitals and welfare centres for permitting us to use their records.

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OESOPHAGITIS*

BY

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You are no doubt aware that at the moment a great interest is being taken in inflammation and chronic ulcer of the lower oesophagus, and that in a sense they are new. In another sense they are not, for many of the things we are now considering have been described before. For instance, patients have always complained of their symptoms, though doctors may have misinterpreted them or brushed them aside because they did not recognize the pattern. Pathologists have described chronic ulcers from time to time for over a hundred years. Radiologists have been examining the lower oesophagus for forty years. Endoscopy is even older, having been first introduced eighty years ago, though it is the recent increase in its use that has contributed most to our present theme.

We are not, therefore, dealing with a brand-new discovery of which the profession has no previous knowledge. In such a case we would have no prejudices, and learning about it would be the relatively simple process of absorbing facts. But the lower oesophagus is ground that has been worked over many times before. Everyone knows something about it. In the last decade new facts have been contributed, but mostly we have been re-examining old evidence and looking at familiar things in a different way. This is a complicated process which people move through at different speeds. Some are apt to cling to the views they have held and found comfortable. Others delight in rearranging the counters of our knowledge without necessarily adding to them. At the moment we are in a period of considerable confusion. Old beliefs have been challenged. New ones have been offered but have not yet taken their place. No doubt all this will soon get stabilized in an orthodox opinion, but in the meantime an interim report may be

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valuable even if it will soon be wrong. This sorting out of ideas has great practical importance, even though it may not result in dramatic cures and saving of life. Confusion breeds uncertain diagnosis, and a patient without a firm diagnosis is often worse off than without a cure.

Symptoms

The symptoms of oesophagitis are pain in the lower chest and heartburn. The chest pain is central and is described as being like wind, food stuck, or a pressing or burning sensation. When it is more severe it radiates to the left side and back. When it is severe, and especially when it is chronic, there is a constant feeling as if someone's knuckles were pressed into the back of the left lower chest. Usually it has no clear-cut relationship to feeding, though there is often enough to make the patient think it is a dyspepsia. Occasionally it quickly follows the taking of food, and then presents as a dysphagia. Sometimes dysphagia is severe and there may be obstruction. The pain lasts for periods of about half an hour. It does not show periodicity over weeks or months like a peptic ulcer.

Heartburn is a lay term, and is used by patients to describe various symptoms. I think most doctors would expect it to mean a burning or hot pain that rises from the upper chest into the throat and may spread into the jaws and mouth and be accompanied by flushing of the face and watering of the eyes. It feels as if some acrid fluid is being forced up the gullet, and the patient swallows repeatedly to keep this down. Regurgitation may indeed occur, but it is not common, and regurgitation is not necessarily accompanied by heartburn. It is most characteristic in this syndrome when it is made worse by stooping. Patients give up scrubbing floors, gardening, or putting, and dread the time they go to bed. Heartburn and chest pain may occur separately or together, and it is difficult to say where one begins and the other ends. There is no point in trying to make this distinction, for they are both oesophagus pains. Chest pain is felt when the lower part is affected and heartburn when it is the upper. One other common feature may be added, and that is rosacea in women. Several of my patients have been under dermatologists for years, and its association with indigestion is of course well known.

These symptoms are as stereotyped as those of peptic ulcer, and one finds patients describing them again and again, once one's ear is attuned to recognizing them. But they are not generally recognized, and we may well inquire why this is so. I think there are two main reasons. The first is that they are the well-known accompaniments of other obvious disease in whose symptomatology they lie buried, or else they are only a minor nuisance and are not taken seriously by patient or doctor. They are, for example, very common in peptic ulcer patients. They are so common with cholecystitis that they are part of the characteristic syndrome. They may also occur as part of almost any dyspepsia. In their minor forms they have been experienced by most people at odd times. In pregnancy they are usual, and, like sickness and swollen legs, are passed off as one of the things you must expect to get. The second reason I suggest for their lack of recognition as a clinical entity was the difficulty of associating them with any organ, pathological change, or objective sign. Even if the lower oesophagus was suspected, there was until recently no means of proving it. The change came when surgeons and anaesthetists mastered the technique of operating safely within the thorax, and it was the surgeon's use of the oesophagoscope that taught the physician to understand what his patients were complaining about.

The Disease

I will now give a dogmatic account of the disease oesophagitis. This account contains much that is believed to be true and a good deal that needs to be proved. The criticism can come later.

The first event is the repeated bathing of the lower end of the oesophagus with gastric juice. This is normally prevented by some mechanism the nature of which is disputed. This is discussed below. In the meantime we may notice that the mechanism—whatever it may be—is liable to be upset when there is any change in the anatomy of the approaches to the stomach. It then becomes incompetent. For example, the oesophagus may be congenitally short, so that part of the stomach lies in the thorax. More commonly there is a hiatus hernia, with a portion of the stomach intermittently or permanently pushed into the chest. Hiatus herniae may also be produced by large abdominal tumours, of which the uterus in the later months of pregnancy is the most notable. The approaches may be interfered with by surgery or destroyed by a growth. Lastly, in a few cases it can be shown that the lower end of the muscular oesophagus is lined by gastric epithelium which may therefore lie above the closure mechanism.

These anatomical abnormalities are not always accompanied by functional incompetence. Nor, on the other hand, is incompetence always due to them. In those cases in which incompetence exists without them, it is presumed that there is some reflex or intrinsic disturbance. This is held to account for the symptoms associated with cholecystitis and early pregnancy, and cases in which barium can be seen to flow back from the stomach with changes in posture.

The effect of constant bathing with acid pepsin is to inflame the gullet, first at the lower end. This is shown by the fact that subsequent regurgitations of acid become painful, whereas normally they are painless. In the early stages nothing abnormal can be seen with the oesophagoscope, and this state may be compared with the soreness that can be felt in a tongue long before reddening can be seen. Later the normal bluish-pink ground, crossed by the tracery of small veins, is replaced by a uniform velvety scarlet which bleeds easily when touched. Then white patches of desquamating epithelium appear. These are followed by superficial oval ulcers with a white or yellow slough surrounded by a red line of inflammation. Intermittent spasm while feeding may sometimes be seen radiologically at this stage.

The erosions heal and recur and nearly always remain superficial. Occasionally one will penetrate deeper and become a chronic ulcer. It is accompanied by much inflammatory oedema, which gradually becomes organized. The thickening is obvious enough at operation or post-mortem examination. At this stage radiological changes become more striking, and it is easy to see the thin trickle of barium through the stricture and the crater projecting sideways like an ulcer in the stomach. These ulcers are often not visible through the oesophagoscope, or only the upper end is seen, because they are buried in the stricture. This accounts for the difficulty there may be in deciding whether the lesion is benign or malignant, or whether there is an ulcer at all. Above it there will be seen the usual inflamed segment with superficial erosions running down between the mucosal folds into the narrow part.

The final outcome is a fibrous stricture. The chronic ulcer may heal and the inflammation above it disappear. It is seen as a smooth funnel both radiologically and with the oesophagoscope.

Prognosis

The outlook when the disease is due to pregnancy, cholecystitis, or cancer is largely determined by cause. In those cases due to primary disturbance of the mechanism it is as follows. The majority of patients who have symptoms and demonstrable reflux get no further complications. It is true that the symptoms may last intermittently over many years or even for the rest of the patient's life. Apart from occasional partial remissions there is little tendency for them to stop. They may get worse, usually gradually, but do not often get better. Those who get a subacute or chronic ulcer with severe painful dysphagia or an obstruct-

ing stricture are very few indeed. It is a possible outcome, but so unlikely that it need hardly be taken into consideration when assessing the patient's future. That does not mean that fully developed cases will not be met with. It means that they are usually seen when already in the later stages. If patients came earlier to their doctors and the oesophagitis were recognized, then more of them would be observed acquiring the later complications. On the other hand, one may be surprised to see a patient with an advanced stricture who has a history of only slight symptoms lasting less than a year. A similar lack of correspondence between the severity of symptoms and maturity of the lesion is seen often enough in ulcers of the stomach.

Criticism

This account now needs modifying. In the first place how certain is it that acid pepsin causes the inflammation? We should be on our guard against a too easy assumption here, for, although it is often held to be the cause of ulcers and inflammation in the stomach, duodenum, and parts of the intestine that may be anastomosed to the stomach, there are still difficulties in this simple view. This question cannot be discussed here, and it is sufficient to point out that we have not got a firm pathology of the ulcerating effects of acid pepsin that could be applied directly to the lower end of the oesophagus. That it has an important role few would doubt, for the frequency with which reflux is accompanied by inflammation is very suggestive and treatment that prevents it is successful. Nevertheless, reflux can occur without inflammation. Many people regurgitate regularly without symptoms, and hiatus herniae are quite common without any disability. Some infants get penetrating ulcers in a remarkably short time, but most regurgitate happily without them. As with peptic ulcer in the stomach and duodenum, we are forced to the same conclusion—that even if acid pepsin is a factor the local state of the epithelium is equally important. There must be some other factor here which prevents inflammation, or fails to prevent it with the same conditions of peptic activity. Despite much research there is no clear understanding of its nature in the stomach and duodenum, and, so far as the oesophagus is concerned, we have got no further than seeing that such a factor is a necessary logical postulate.

This leaves us in the rather unsatisfactory position that the only factor which we know about is the acid pepsin, so that when symptoms are heard or inflammation is seen we look hard with a fixed determination to see what we ought to. The old view of gastric rests in the oesophagus is an example of forcing things too far. When no short oesophagus or the like could be shown, it was held that it was these rests which produced the secretion to inflame the surrounding mucosa, or themselves ulcerated, as they do in a Meckel's diverticulum. It has now been shown that, although such rests are common, they are minute in size and hardly seem adequate to cause trouble, quite apart from the fact that they mostly occur in the upper end. A modern tendency, also resulting from preoccupation with acid pepsin, is to exhort the radiologist to produce some reflux by tipping, stooping, and abdominal pressure. Often he can, but I think it can still be questioned how much bearing these manœuvres have on the normal life of the patient. Perhaps we demand too much of ourselves in this respect, for oesophagitis is a chronic condition which may often develop slowly from intermittent irritation. Even if acid pepsin is the irritant we should not necessarily expect always to demonstrate it on the few occasions that we can examine the patient.

We are surely on firmer ground when we say that acid is the commonest irritant that precipitates pain once oesophagitis is established. The effect of posture is very suggestive. Also the ulceration that may occur with cardiospasm, but which acid never reaches, is never painful. But acid regurgitation often occurs from time to time without these pains. The most obvious example is in vomiting. We must therefore suppose that the inflammation sensitizes the pain nerve endings so that the normally innocuous acid becomes a painful stimulus. This would be called tenderness in an accessible structure, and we see the same thing with other viscera—when, for example, normal urine becomes an irritant in urethritis. In some cases, especially when inflammation is severe, patients will complain of continuous pain, and it is difficult to believe that their gullets are subjected to a continuous bath of acid. It seems more likely that, as with other parts of the body, a certain degree of inflammation is itself enough to stimulate the pain nerve endings without any adventitious irritant. It is somewhat surprising that the mechanical stimulus of swallowed food is usually painless, for it is only in the most severe and chronic cases, in which there is a chronic ulcer and inflammatory narrowing, that a painful dyspepsia is at all common.

Even if it be granted that these are the ways that pain is caused in oesophagitis, one must not assume that all similar pains are due to the same cause. Heartburn, for example, can occur with achlorhydria; swallowed corrosives feel the same; and in other cases spasm may play a part. The identity of the sensation with various stimuli can be shown experimentally—the pain feels the same whether it is caused by faradic shocks, inflated balloons, acids, alkalis, or neutral irritants.

Some Speculations

A question now arises. Should the physician, when he hears these symptoms, have a mental picture of a red inflamed mucosa? Unfortunately it cannot be definitely answered, though probably he should. Although oesophagoscopy is 80 years old, it was for long a dangerous and uncommon examination. Even to-day, with the great increase in its use, it is mostly employed by surgeons for presumed surgical conditions. The exceptions are the American oesophagoscopists, of whom Chevalier Jackson is the chief. In 1929 he stated: "When the time shall come when every patient with the slightest discomfort or abnormality in swallowing, every patient with pain or discomfort back of the sternum, every patient with gastric haematemesis, every patient with regurgitation, 'heartburn' or 'water brash' is examined oesophagoscopically, peptic ulcer in the oesophagus will be found less rare than it is now thought to be, though it is probably not a common disease."

We may add: "What would we learn about simple oesophagitis?" This day has still not come after 20 years, and it may be argued that it never should. In the meantime we cannot tell how common oesophagitis is, how often it exists without symptoms, or how often symptoms mean oesophagitis.

These speculations are of considerable importance, for what the physician tries to do depends on his mental picture of the pathology. The fairly recent change in attitude to gastric and duodenal pains is a case in point. In the days when he believed pain was caused by hyperacidity, hypoacidity, and so on, his diagnostic tests were concerned with studying changes in the juice, and his rational therapeutics were chemical and surgical procedures that altered it. But when the ulcer came into its own again our attitude changed. Our diagnosis now consists in the anatomical demonstration of a deformity, and our treatment tends more and more to its surgical removal.

We will now pass from this discussion of how gastric juice inflames the oesophagus to consider how it gets there. This is quite the most confused part of the subject. Partly this confusion is due to what has been thought in the past and which still remains with us as a legacy. I had hoped to put these in proper perspective by considering the history of their development in detail, but this is unprofitable. I will content myself with two observations, which I hope will clear up some misapprehensions. The first concerns the short oesophagus. It was originally held that this was always a congenital failure of descent. The cases were studied *post mortem* and were advanced. Later, when

radiologists began to show that the stomach could often be seen in the thorax, it was supposed that the cause was still the congenital shortening. It is not denied that such cases do exist, but they are now held to be uncommon. It is agreed that the fault in most cases in which the stomach is seen in the thorax is a hernia of the diaphragm.

The second point is the question of scar contraction of the oesophagus. During the war, when thoracic surgeons began to deal with advanced cases, some were seen in which the oesophagus appeared to shorten. This gave rise to the view that the stomach was drawn up by scar contraction of the oesophagus. This appearance was in fact due to an extension upwards of the stricture, and I think it is now generally agreed that scarring does nothing but narrow and fix the oesophagus.

The Question of Reflux

We come back, then, to the normal mechanism that prevents reflux, and it would be logical in discussing its pathology to describe how it normally works. Unfortunately this is not fully understood. There are three hypotheses current. The first is that the right crus of the diaphragm acts as a pinch-cock, either by squeezing the gullet or by pulling it downwards and backwards. This hypothesis is supported by the fact that herniation is often accompanied by incompetence, and fixing the stomach back into the abdomen by cure. On the other hand, hiatus herniae are not always incompetent, and it cannot be convincingly shown that the point of radiological closure corresponds with the crus. In any case, there is normally squamous mucosa in the short part of the oesophagus in the abdomen, lying below the pinch-cock. Lastly, we do not find reflux when the diaphragm is paralysed.

The second hypothesis is that the oblique entry of the oesophagus into the stomach, together with the arrangement of the intrinsic muscular fibres, constitutes a valve. This is an old view based on anatomical studies, and it is difficult to show that it really works. It would account for the failures of the pinch-cock hypothesis, but does not easily explain its successes. The last hypothesis is the suggestion that neither of these is satisfactory, and that there may, after all, be a functional sphincter at the lower end of the oesophagus, even though it cannot be demonstrated anatomically. The field, in fact, is open, and these remarks have been made not to show how the mechanism works but to point out that there is no answer to be had from asking. It is a subject that does not perhaps directly concern the physician, but it is of the first importance to the surgeon who is called upon to make a repair.

Clinical

Now let us leave this discussion and consider what our attitude may be when confronted with a case. Whether these views will be found to be right or wrong, we have to manage our patients with the knowledge at our disposal.

There is always a tendency, in the enthusiasm of recognizing something new, that one may concentrate attention on it to the exclusion of what is old and humdrum. As a matter of self-discipline, then, there are three things to be remembered. First, that these symptoms are often secondary to pyloric ulcer, cholecystitis, or cancer, and that these must be excluded. Secondly, that the chance finding of a hiatus hernia, short oesophagus, or the like is an abnormality to be left undisturbed unless it is producing symptoms. Finally, the symptoms must be the right ones if they are to be attributed to the abnormality found. Patients complain of so many unclassifiable pains in the belly that the physician is apt to grasp at any straw that floats by. This is harmless enough if it merely consists in giving a diagnosis that the next generation will reject. But when he holds an anatomical abnormality responsible for symptoms we inevitably start putting it right by surgery. This may lead to meddling, as the history of appendicectomy, visceroptosis, and much of gynaecology shows.

Routine radiology will show the grosser abnormalities of hernia, reflux, stricture, and spasm. Spasm may be diagnosed as cardiospasm; but this is sometimes a dangerous diagnosis to make, especially if there is pain, for the spasm may be due to an inflammatory or a neoplastic lesion. Stricture is clearly seen, and often there may be an ulcer crater as well. In such cases it is not always easy to be certain, even with oesophagoscopy, that there is no cancer, and exploration through the chest may be necessary. What to do when there are no radiological changes is more difficult to decide, and it depends on the circumstances of the case. If there are mild symptoms a diagnosis can be made on these alone. Often there is a background of uncertainty and of conflicting diagnoses having been made, and in these it is essential to get some support for one's suggestion. An oesophagoscopy is final if inflammation is seen, though it is not yet certain how often this will be found as the milder cases are examined. When the symptoms are severe enough to warrant surgical treatment the emphasis is on finding an anatomical abnormality. It will of course be helpful to have seen inflammation through the oesophagoscope, for this confirms the diagnosis and shows that the trouble has advanced to this degree. But, since the only radical cure is the repair of the mechanism, the most important thing is to demonstrate radiologically that it is faulty. It is in these cases that the radiologist may be encouraged to produce a hernia or reflux by stooping and compression, and the examination may be justifiably repeated, for these things do not happen every time.

Treatment

The most effective treatment is surgery, and the first duty of the physician is to decide whether this is justifiable. Except in the case of stricture or penetrating ulcer, this decision should be based entirely on the severity of the symptoms. Although we believe that strictures and ulcer are the sequelae of simple oesophagitis, this is by no means certain. In any case, it is a rare complication and much less likely to affect the patient than are the natural hazards of surgery. The decision will be affected to some extent by the kind of repair that the surgeon may be expected to do. Thus it will be easy and sure when a hiatus hernia is found. It will be less sure when reflux is in doubt, and less easy when the oesophagus is congenitally short.

In most cases it will be enough to let the patients know what they have and that it will cause no harm. They may also be comforted by the knowledge that there is always surgery to fall back on if life should become too miserable. Simple measures such as taking small feeds, small amounts of alkali, and sleeping upright are sensible, but, excepting the last, do not make much difference. I do not know that anyone has tried repeated applications of astringents through the oesophagoscope since Chevalier Jackson recommended it 20 years ago.

Surgery in the case of oesophagitis from hiatus hernia consists in fixing the stomach below the diaphragm. In most cases it is successful. Stricture if untreated is a fatal condition. Dilatation with bougies will temporarily make swallowing possible, but it has two overriding drawbacks. The first is that the dilated stricture remains open so that further reflux occurs and the whole cycle of inflammation, ulceration, and stenosis is repeated. The other is that sooner or later a false passage will be made, so that, as Charcot said, "They that live by the bougie will die by the bougie."

Stricture and penetrating ulcer require surgical removal. The lower end of the oesophagus is now well within the limits of practical surgery, though the middle reaches are still dangerous ground even with the expert. If the oesophagus can be drawn down and anastomosed to the stomach below the diaphragm, then reflux may not recur. If it cannot, the stomach must not be drawn up into the thorax, for this again leaves the patient with the stage set for return of the trouble. Various devices are being tried to avoid

this, such as using an end of the jejunum or a tube made from the greater curve of the stomach. None of these methods has yet reached the orthodoxy of a set piece.

Conclusion

Finally, let me take stock of our position. We have got to the stage of attaching symptoms to an organ, and we believe that it is inflammation of the organ that causes them. This union is due to the surgeons, but before the physician can make proper use of it he must know how often these symptoms do in fact mean what we think. We need a wide endoscopic survey of cases of chest pain and heartburn in the way that Chevalier Jackson foreshadowed. We have also got to the stage of discussing the pathological mechanisms that cause this change. Our views are mostly based on the investigation and treatment of advanced cases, and we may hope that further experience will give us clearer knowledge of what goes wrong in the early ones.

DETERMINATION OF CHOLINESTERASE ACTIVITY IN HUMAN BLOOD

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In a memorandum on the signs, symptoms, and treatment of cases of poisoning resulting from the absorption of the organo-phosphorus insecticides, the British Medical Association in 1951 drew attention to the value of a knowledge of the level of blood cholinesterase in making the diagnosis and following the recovery from the effects of poisoning. Following the work of Callaway, Davies, and Rutland (1951) on the levels of cholinesterase in a normal population, Barnes and Davies (1951), using these results, have shown that lowering of the blood cholinesterase levels could be detected in workers exposed to these insecticides who showed no clinical symptoms.

The estimation of the blood cholinesterase is not a standard procedure in clinical pathology, and it is the purpose of this paper to summarize the available methods for making those determinations and to describe in detail a method suitable for adoption in a general clinical laboratory.

Although "parathion" and "schradan" are poor inhibitors of cholinesterase *in vitro*, they both owe their poisonous properties to the fact that after absorption in the animal body they are converted into active inhibitors of this enzyme (DuBois *et al.*, 1950; Gardiner and Kilby, 1950; Aldridge and Barnes, 1952), and the symptoms of poisoning so produced seem to follow from the inhibition of cholinesterase. There is evidence that the blood cholinesterase is lowered before that in the tissues (Hobbiger, 1951), and it is the loss of the cholinesterase at nerve endings and in the central nervous system that is responsible for the symptoms of poisoning.

Determination of cholinesterase levels in blood can be of value because: (1) The early symptoms of anti-cholinesterase poisoning are almost wholly local in character and are not necessarily indicative of systemic absorption. Systemic absorption is much more insidious, and the only convenient measure of such a process is the level of cholinesterase in the blood (Davies *et al.*, 1951, unpublished results). (2) A fall in the cell or plasma cholinesterase level may well be the first indication of absorption of these substances (Barnes and Davies, 1951). (3) After poisoning, the blood enzymes will remain at a very low level until the regeneration of new enzyme, and this is very slow. The red-cell enzyme reappears at approximately 1% a day, although the plasma enzyme reappears more quickly (Grob *et al.*, 1947). During this period, when the blood enzymes are low, an individual is hypersensitive to subsequent doses of anti-cholinesterase (Callaway *et al.*, 1951). (4) Many of the symptoms of poisoning by anti-cholinesterase agents are commonplace in character—headache, tightness of chest, nausea, internal discomfort, etc. Hence the determination of cholinesterase blood levels may well be of much value in the differential diagnosis in cases of mild poisoning.

Determination of the Cholinesterases in the Blood

The cholinesterase in human erythrocytes differs from that present in the plasma. These two enzymes possess quite different properties; a knowledge of the properties is desirable in order to understand fully the problem of their assay. This aspect has been well reviewed by Whittaker (1951).

In view of the lack of sensitive or specific methods for the determination of the acetic acid or choline produced during the hydrolysis of acetylcholine by the cholinesterases, most methods have been based on the unspecific measurement of an acid produced.

Warburg Manometric Technique.—This technique, developed by Ammon (1933), is based on the measurement of carbon dioxide liberated from a bicarbonate buffer by the acetic acid liberated by hydrolysis of acetylcholine. Details of this method are available in several recent publications (Adams and Whittaker, 1949; Aldridge, 1950; Callaway *et al.*, 1951). Although it is a most elegant and accurate method it is more suited to research work than the routine determination of large numbers of specimens. The apparatus is expensive and the technique rather specialized.

Continuous Titration Method (Stedman *et al.*, 1932).—In this method the acetic acid formed is continuously neutralized by the addition of alkali. The *p*H of the reaction system is thus maintained constant. Although the apparatus required is found in most laboratories (*p*H meter, microburette, constant-temperature bath) and the procedure is simple, only one determination may be carried out at a time, and the procedure is very tedious. It is not recommended for routine estimations.

Colorimetric Method of Hestrin (Wilson and Bergmann, 1950; Diggle and Gage, 1951).—Hestrin (1949) applied a method for the determination of esters to the determination of acetylcholine. Cholinesterase activity may therefore be determined from an estimation of the acetylcholine present before and after enzymic hydrolysis. This method suffers from the inaccuracy usually associated with methods based on the measurement of small differences in relatively large amounts. Also the rate of removal of acetylcholine is not a linear function of enzyme concentration.

Electrometric Method of Michel (1949).—This is essentially an indirect method of measuring cholinesterase activity by the fall in *p*H of a barbitone/phosphate buffered system due to the acid produced. This empirical buffer system has been devised so that the fall in *p*H is linear with time even though the activity of the enzyme is being lowered by the fall in *p*H itself. The method has been shown to correlate well with the standard Warburg technique (Hamblin and Marchand, 1951). The apparatus required is a *p*H meter reading to 0.01 unit and a constant-temperature bath. The actual procedure involves only two *p*H readings, one

before and one after hydrolysis for a given time. Since up to 40 estimations may be carried out together, the method is well suited for routine determinations. Hitherto all analyses have been carried out upon cells or plasma (Callaway *et al.*, 1951). This is not absolutely necessary, for, despite differences in the two enzymes, determinations upon whole blood may be satisfactorily used for the routine detection of the possible systemic absorption of the anti-cholinesterase insecticides. In the event of a given specimen yielding a low result, a venepuncture sample should be obtained and the cells and plasma separately examined.

Experimental Details of the Electrometric Method (Michel, 1949)

Reagents

1. Buffer No. 1 (for erythrocytes):

0.02 M sodium barbitone	4.1236 g.
0.004 M potassium dihydrogen phosphate ..	0.5446 g.
0.60 M potassium chloride	44.730 g.

Dissolve the reagents in 900 ml. of distilled water and determine the *p*H. Add 0.1 N HCl until *p*H 8.10 is reached at 25° C. (approximately 15 ml. is required). Dilute to 1 litre.

2. Acetylcholine substrate for erythrocytes (0.11 M). Acetylcholine chloride, available from Roche Products Ltd. in 0.1-g. ampoules, has been found suitable. Dissolve 1 ampoule in 5 ml. of water.

3. Buffer No. 2 (for plasma and whole blood):

0.006 M sodium barbitone	1.2371 g.
0.001 M potassium dihydrogen phosphate ..	0.1361 g.
0.30 M sodium chloride	17.535 g.

Prepare as for buffer No. 1 for erythrocytes, but in this case adjust the *p*H to 8.0 (approximately 11–12 ml. of 0.1 N HCl is required).

4. Acetylcholine substrate for plasma and whole blood (0.165 M). Dissolve 0.1 g. (1 ampoule) in 3.3 ml. of water.

5. 0.01% w/v saponin.

6. 0.90% w/v sodium chloride.

7. Potassium oxalate as anticoagulant.

Equipment

The minimum equipment required is a *p*H meter reading to 0.01 unit, a constant-temperature bath at 25° C., and a quantity of wide-bore medium-walled short tubes of 20 ml. capacity. However, for routine examination of many samples it has been found convenient to have an attachment which allows the quick and yet safe movement of the glass electrode from one tube to another. A slight scratch on the glass electrode will cause irreparable damage.

1. *pH Meter.*—Any standard instrument which may be read to 0.01 unit is suitable. We use a Cambridge battery-operated model.

2. *Electrodes.*—Calomel half-electrode Muirhead type with a long flushing tube, and a dip-type glass electrode with a 3-ft. (0.9-m.) lead.

3. *Constant-temperature Bath.*—An ordinary laboratory rectangular water bath with a temperature control of ±0.2 degree and capable of being operated at 25° C. is quite adequate. The bath is fitted with an electrode-holder which can be moved sideways as well as forwards and backwards. It consists essentially of two pillars, A A (see Diagram), connected by a rod, B. The bottom of each pillar is bent at right angles. A piece of angle brass helps to form with the bottom of the pillar a sliding bracket which permits backward and forward movement of the holder across the width of the bath. A slotted bracket, which carries a vertical rod, C, capable of lateral movements, also carries the actual bracket which supports the holder, D. This can be moved vertically on the rod C. This device permits the controlled movement of the electrode in three dimensions: it is necessary in order to protect the electrodes, which may easily suffer irreparable damage by rough contact with the sides or bottom of the reaction tubes.

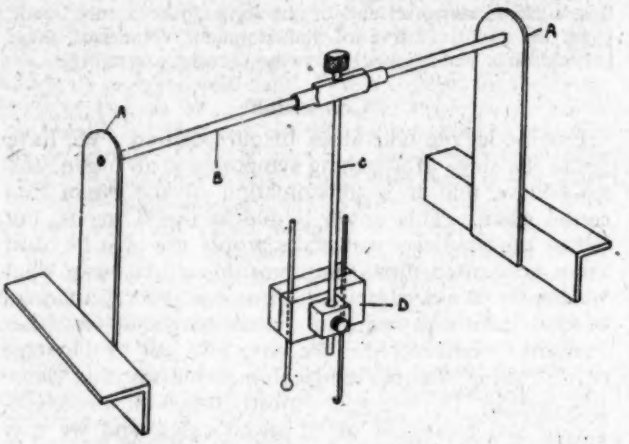

Diagram of movable electrode-holder.

4. *Tubes.*—To facilitate the easy and safe manipulation of the electrodes in the reaction tube, tubes 2 in. (5 cm.) high and 1¼ in. (3.1 cm.) in diameter, with medium-thick walls and constructed of soda glass, were used. (These can be obtained from Messrs. Hearson and from Messrs. Baird and Tatlock.)

Collection and Preparation of Blood Samples

Provided the blood is not clotted the cholinesterases are quite stable in whole blood. If analyses on erythrocytes and plasma separately are required no haemolysis should be present, and the cells should be separated without delay—preferably within 24 hours.

For whole-blood analyses enough blood may be obtained from finger-tip or ear-lobe punctures. However, for a determination on erythrocytes or plasma a venepuncture is required to obtain the necessary 5 ml. Details of the precautions necessary to obtain samples free from any of the defects mentioned above are given by Harrison (1943).

For the separation of erythrocytes and plasma the following standard procedure is recommended: Centrifuge approximately 5 ml. of oxalated blood at 2,000 r.p.m. for 15 minutes (800 *g*). Separate plasma and wash cells twice with saline, finally centrifuging for 20 minutes at 800 *g*. Remove supernatant, thus leaving a preparation of washed cells which have been packed under standardized conditions.

Procedure for Enzyme Estimation

As mentioned above, the method is precisely the same for whole blood, cells, and plasma. The only differences are to be found in the composition of the buffer solution and the concentration of the acetylcholine solution. The following procedure is for either whole blood or plasma; the necessary modifications for cells are included in parentheses: (1) 0.1 ml. of blood, plasma, or cells is measured in an appropriate McClean's blood pipette and transferred to 10 ml. of a mixture of equal volumes of buffer No. 2 (or buffer No. 1 for cells) and saponin solution contained in a reaction tube in the constant-temperature bath at 25° C. (2) Add 1 ml. of 0.165 M acetylcholine chloride (0.11 M for cells). (3) Note the time, and exactly half a minute after the addition of substrate note the *p*H. (4) Exactly 60 minutes later take the *p*H reading again. (5) The difference in *p*H readings, △ *p*H/hr., is a measure of enzyme activity, and is called the "cholinesterase number" (ChE No.) which is the fall in *p*H produced by 0.1 ml. of whole blood in one hour × 100.

Normal Limits of Whole-blood-cell and Plasma Activity

The interpretation of figures obtained by any of the procedures outlined above is dependent upon a knowledge of the normal variation of these enzymes in health.

For whole-blood analyses—that is, for determination of the ChE No.—data are available only upon young male

Service personnel between the ages of 18 and 30 (Davies *et al.*, 1951, unpublished results). Figures have been obtained from 230 males from the armed Services.

The mean value of the ChE No. was 111. (The coefficient of variation of this series was 12.1.) Thus the normal limits—that is, the fiducial limits—become 87 and 136. Owing to the difference between the red-cell activity of the Service and civilian groups (Callaway *et al.*, 1951), these values are probably too high by about 5 to 7%, and accordingly a sounder estimate of the lower limit may be taken as 80.

No observations have been made upon the "personal" variation of the ChE No. The relevant data of Callaway *et al.* (1951) may, however, be used to provide an estimate of what must be the difference between two determinations in the same person of the cell (or plasma) enzyme which will indicate departure from normal limits. The differences referred to above for the red-cell and plasma enzyme respectively are 15 and 20% of the higher of the two values. Thus even if the plasma figures were applied to the ChE No. —that is, even if the wider limits were applicable—there still remains a substantial margin between the recognition of abnormal deviation and the onset of those symptoms which indicate the development of lethal processes. The ChE No. must certainly be decreased to below 40% of its initial value before any definite clinical symptoms due to systemic absorption occur (Davies, 1951, unpublished results).

Normal limits for the whole-blood, red-cell, and plasma enzyme are summarized in the Table.

	Cholinesterase Number	
	Lower Limit	Upper Limit
Red blood cells	51	100
Plasma	40	100
Whole blood	80	129

Variations in Blood Cholinesterase Due to Disease

There are many references in the literature to the variation of both cell and serum cholinesterase. Most of the information, however, has not been really substantiated, and in only two conditions is there clear-cut evidence correlating a lowered cholinesterase with the disease. Thus the position has been accurately summed up by Augustinsson (1948) in these words: "The cholinesterase concentration of the blood has been widely studied in order to correlate the enzyme activity with various pathological conditions. . . . The mass of data obtained, however, has not allowed of any conclusions as to the relation between ChE activity and the disease investigated."

Reduced serum cholinesterase values have been found in liver disease by a number of workers (McArdle, 1940). Hutchinson *et al.* (1951) have recently shown that the plasma enzyme is very significantly lowered in malnutrition. There is little firm evidence to indicate any great variation during disease in the amount of cholinesterase in red cells.

Summary

The suitability or otherwise of the various common methods for the routine estimation of cholinesterase is described.

It is suggested that the "cholinesterase number" (ChE No.) should be determined as a routine screening test, using the Michel electrometric method for the purpose, and that any departures from normality should be investigated in a more orthodox manner by determinations of red-cell and plasma cholinesterase, also using the electrometric method.

Details of techniques for obtaining blood samples and a description of the reagents, apparatus, and methods of performing the enzyme analysis are given.

The problem of normal values of the ChE No., together with the population and personal variation of both enzymes, is discussed. Values of normal limits are included.

In only two pathological conditions—liver disease and malnutrition—is there firm evidence that the level of serum or plasma cholinesterase is lowered. There is no clear-cut evidence that the level of the red-cell enzyme is seriously influenced by disease.

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CARCINOMA OF THE OESOPHAGUS

THE DIAGNOSIS AND SURGICAL TREATMENT OF 159 CASES

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This paper presents the clinical aspects and pathology of 159 patients suffering from carcinoma of the oesophagus who were admitted to Hammersmith Hospital during the past nine years. We have reviewed the surgical results during the period 1946–9 inclusive. The late Professor Grey Turner, who played such a great part in laying the foundation of oesophageal surgery, was in charge of the cases before 1946, and since then one of us (R. H. F.) has continued with the management of this condition.

Major discoveries and minor modifications during the past few years have resulted in a steady improvement in the surgical results, and attention is drawn to those adjuncts that have been of particular help.

Clinical Aspects

Age and Sex.—Of the 159 patients, 72% were men and 28% women. The average age of the men was 63 years and of the women 64. The youngest patient was a man, aged 22, with a resectable growth of the upper third of the oesophagus. The oldest patient was a woman, aged 81, with an inoperable growth situated in the middle third of the

oesophagus. The oldest patient upon whom a successful resection was performed was 76 at the time of the operation. The age group most affected was that between 60 and 70 years, and comprised 34% of the patients. The age group next in frequency of involvement was that between 70 and 80, and comprised 31% of the patients.

Duration of Symptoms Before Admission.—Sixty per cent. of the patients were aware of symptoms for three months or less before admission. One patient, who had suffered for two years from dysphagia, died six days after admission and a necropsy showed an extensive growth ulcerating through the trachea. Six patients stated that symptoms relating to their condition had been present for over one year.

Site of Growth.—Sixty per cent. of the patients had growths situated in the lower third of the oesophagus, 28% in the middle third, and 12% in the upper third.

Earliest Symptoms.—Dysphagia is the commonest first symptom of the disease (see Table I). This symptom was noticed first by 87% of the patients. Pain occurred in various sites, including the epigastrium, upper abdomen, behind the sternum, in the back, and in the neck. Weakness was noted by four patients as the initial symptom, hiccup occurred in three patients, and regurgitation of recently swallowed food was experienced by three other patients. Other rare presentations are described more fully below.

TABLE I.—*Earliest Symptom Observed by Patient in 159 Cases of Carcinoma of the Oesophagus*

Symptom	No. of Patients	Symptom	No. of Patients
Dysphagia	137	Hiccup	3
Epigastric pain	6	Lump in throat	2
Upper abdominal pain	2	Loss of weight	1
Substernal pain	3	Anorexia	1
Back pain	1	Lump in femur	1
Pain in the neck	1	Haematemesis	1
Weakness	4	Irritation in throat	1
Regurgitation	3		

Physical Signs.—Loss of weight is the most constant finding on clinical examination. Examination of the neck may show the presence of malignant nodes. These were palpable in six patients, though in two of them the growth was situated in the thoracic part of the oesophagus, as subsequent biopsy confirmed. Evidence of intra-abdominal spread in the form of a palpable or nodular liver was present in 12 cases.

Symptoms in Detail

The symptoms shown in Table II have been chosen for more detailed consideration; most of the patients had a triad of symptoms—dysphagia, regurgitation, and loss of weight.

TABLE II.—*Symptoms Complained of During the Course of the Disease*

Symptom	No. of Patients	Symptom	No. of Patients
Dysphagia	153	Anorexia	14
Loss of weight	145	Heightened appetite	14
Regurgitation	104	Cough	23
Pain	66	Flatulence	22
Sense of obstruction	76	Haematemesis	17
Weakness	26	Melaena	5
Constipation	31	Excessive salivation	2

Anorexia was commonly complained of in the case of growths affecting the lower part of the oesophagus, but was not a common feature of upper oesophageal growths.

It was found that 76 patients were aware of an obstruction, and 55 of them gave the correct level of the growth. In 38 out of 66 (53%) patients suffering pain it was situated over the site of the growth.

Involvement of the mediastinal structures may produce pain in the back, but this may occur even from a growth which has not spread beyond the oesophagus; in only 3 out of 16 patients who suffered from pain in that site had the tumour infiltrated beyond the wall of the oesophagus. Back pain should not therefore be considered a contra-indication to operation.

Flatulence may vary in its effect. In 20 patients it relieved or did not cause pain; in two, pain was occasioned by it.

Unusual Presentations

Summaries of the rare presentations of the disease in this series are given.

A woman aged 71 attended another hospital complaining of pain in the left leg and a swelling in the left groin. A biopsy was taken, and the swelling was diagnosed histologically as a fibrosarcoma. The condition was then treated by removing the limb. During the succeeding months masses developed in the groins, neck, and chest. Further examination of the biopsy specimen was then made, and the original diagnosis was discounted in favour of an anaplastic carcinomatous deposit. The primary was not found until after death; it was situated in the mid-thoracic part of the oesophagus. The patient never complained of dysphagia, although scrutiny of her notes revealed that on one occasion she had regurgitated blood-stained material.

A man aged 45 attended another hospital complaining of soreness of his throat. Tonsillectomy was carried out. Dysphagia developed after the operation and pain was experienced at the back of the head and over the left ear. Further investigation then revealed a growth situated in the upper third of the oesophagus.

A woman aged 81 was admitted complaining of colicky lower abdominal pain and constipation for several weeks. Investigations, confirmed by laparotomy, revealed diverticulitis of the colon, and the finding was considered to be an adequate explanation of the symptoms. However, she complained of pain in the left thigh, and an *x*-ray film showed Paget's disease. The patient was discharged, but was readmitted a month later because of pain in the back, in the lower thoracic region; she appeared to be quite ill. Clinical examination now revealed the presence of a swelling in the left femur and enlarged inguinal lymph nodes. A second *x*-ray film disclosed bony destruction occurring in the region of the great trochanter, and a biopsy of one of the lymph nodes showed carcinomatous deposits. The patient's condition continued to deteriorate, and shortly afterwards she died. At necropsy a primary carcinoma of the oesophagus was found, with secondaries in the inguinal lymph nodes and malignant deposits in the femur.

One man was regarded initially as suffering from angioneurotic oedema of the throat. His symptoms were swelling and irritation of the throat. On examination an oedematous uvula was found. The symptoms improved with the use of antihistamine drugs. He subsequently developed dysphagia and vomited blood-stained material, after which a malignant oesophageal growth was proved.

A woman of 63 was admitted as a case of attempted suicide. Dysphagia and increasing fatigue were the causes of the depression, which led to her attempt on her own life. Investigations and a thoracotomy performed at a later stage revealed an inoperable growth of the oesophagus.

A man aged 58 was admitted with a catastrophic haematemesis and rectal bleeding. He died despite rapid blood transfusion. Necropsy revealed an extensive growth of the oesophagus ulcerating through the aorta.

A man aged 68 was admitted to another part of the hospital with a swelling of the right alveolus. An enlargement of the liver was found on examination. Several biopsies were taken, and the histological diagnosis made was adamantinoma. However, his general condition deteriorated rapidly and an alternative diagnosis was made of primary carcinoma of the liver. Deep *x*-ray therapy was begun, but the patient died. At necropsy a primary carcinoma of the oesophagus was found, with secondaries in the liver; the jaw condition was a secondary deposit.

A man aged 71 complained of regurgitation of food for several months and loss of weight. He was admitted to another hospital and investigated by a barium swallow, in addition to the usual routine examination, and was finally

discharged because nothing was found. Several months later he was admitted to this hospital and died soon after admission. The necropsy revealed a malignant growth involving the upper thoracic part of the oesophagus.

We may mention here one patient who was sent to us as suffering from carcinoma of the oesophagus, but who had in fact a primary carcinoma elsewhere. She was a woman, aged 63, who complained of a varying but progressive dysphagia for two months and a loss of weight over the preceding year. On examination hard enlarged glands were palpated on both sides of the neck, and further examination revealed a carcinoma of the right breast. A barium swallow showed a narrowing of the middle third of the oesophagus, but the mucosa appeared intact. Oesophagoscopy confirmed that the narrowing was due to pressure from without. This mechanical compression was in fact caused by malignant mediastinal lymph nodes resulting from the carcinoma of the breast.

Special Investigations

The following examinations were carried out on every patient.

1. *Barium Swallow and Chest X-ray Examination.*—The direct approach to the diagnosis of malignant tumours of the oesophagus is by barium swallow, yet complete reliance must not be placed on it, for it is occasionally inaccurate. In seven patients barium swallow did not reveal the exact diagnosis. Of four overlooked in this hospital, two were regarded as suffering from achalasia. If a lesion is clinically suspect and the barium swallow does not reveal the presence of a growth, oesophagoscopy must be carried out; our last successful resection undertaken was on a woman aged 42, whose barium swallow was reported by the radiologist to be normal, yet oesophagoscopy subsequently performed showed a malignant ulcer, and later, at operation, a growth was seen to extend for 3 in. (7.5 cm.) along the lower third of the oesophagus without causing an appreciable narrowing of the lumen. On routine examination of the chest a secondary deposit is occasionally found in the pulmonary field. In one case a lateral view of the oesophagus showed absorption of the front parts of the bodies of the lower thoracic vertebrae. The use of thicker barium mixtures may outline tumours whose appearance is only doubtfully outlined by the standard swallow, or not at all.

2. *Oesophagoscopy.*—This essential procedure is employed in all cases, and if a growth is discovered a biopsy is performed. No carcinoma of the oesophagus has been missed when it has been employed, and there have been no accidental perforations of the oesophagus.

3. *Examination of Stools for Occult Blood.*—Although an examination of the stools for blood is always carried out, a positive result was obtained in only 18 patients. No reliance should be placed on a negative result.

4. *Examination of the Blood.*—Haemoglobin estimations are made repeatedly so that anaemia may be treated by oral iron or transfusion, according to its degree. We try to avoid a transfusion immediately before the operation. A full blood picture is requested if there are specific indications for it—the presence of enlarged lymph nodes, for example. The level of the plasma proteins is recorded.

5. *Heart and Kidney Functions.*—An electrocardiogram, a blood urea estimation, and a kidney-function test are occasionally requested to corroborate the clinical appraisal of the functions of the heart and kidneys.

6. *Indirect Laryngoscopy, Bronchoscopy, and Sputum Examination.*—These tests are performed if indications are present. The presence of a cough with the production of large quantities of purulent sputum is strongly suggestive of involvement of the lung and possibly the presence of a fistula.

Pre-operative Management

Patients present complaining of varying degrees of dysphagia. A patient allowed to take solid food soon produces a complete dysphagia by occluding the remaining part of the lumen of the oesophagus. Solid food is accordingly withheld and the patient is given hourly feeds of fortified milk, 1 pint (570 ml.) of which contains 1 oz. (28 g.) of calcium caseinate and 1 oz. (28 g.) of glucose, lactose, or sucrose.

On this diet the patient steadily increases in weight and becomes fit enough for operation. If the patient is unable to take fluids and becomes severely ill, a blind jejunostomy or gastrostomy is performed under local analgesia. On the other hand, if the patient is well enough, opportunity is taken at the time of operation to explore the abdomen. Physiotherapists attend daily and teach the patients to expand and clear their chests in order to obtain the maximum respiratory capacity and function. Penicillin is given for 48 hours before and after the operation to lessen the incidence of pulmonary infection. When the patient is ready for operation 6 pints (3.4 litres) of blood are cross-matched and held in readiness. A saline drip is begun before the patient is taken to the theatre.

Infected teeth are treated by local cleansing. Wholesale extractions should be avoided.

Treatment

It is impossible to particularize on the respective radical procedures employed for each part of the oesophagus, but the following general principles are customarily followed.

1. Operability

Absolute contraindications to excision are involvement of the air passages or evidence of distant dissemination. In the absence of these, exploration should be undertaken and the operability reassessed at thoracotomy. General debility is no bar to exploration, provided that enough nutrition is afforded before operation by the use of fortified milk. It has been stated elsewhere that growths which cannot be separated by blunt dissection are inoperable, but we have employed sharp dissection where necessary, with frequent success.

2. Operative Procedures

Our main objective in all operations has been the restoration of normal swallowing, and in the radical procedures we hope also that we have given the patients some chance of complete cure, however slight.

Growths at the lower end of the oesophagus which involve the cardia are treated by block dissection of the stomach, together with the spleen, omenta, and tail of the pancreas, through a thoraco-abdominal approach, according to the method so well described by P. R. Allison and J. Borrie. Restoration of continuity is effected by oesophago-jejunostomy, employing an undivided loop of small bowel, if possible, or, if that is impossible, by fashioning a Roux anastomosis en-Y.

Carcinomata situated in the lower half of the thoracic oesophagus which did not involve the cardia were exposed through a left abdomino-thoracic approach made at a slightly higher level. If resection was possible, anastomosis was effected by bringing up the stomach, with its vascular arches preserved, and anastomosed to the oesophagus below the aortic arch, provided there was enough healthy oesophagus well clear of the growth below the arch. Although the mortality may be increased by a supra-aortic anastomosis, it is nevertheless better to face it rather than risk an unsatisfactory anastomosis made close up under the arch.

It is not certain which is the best method of treatment for growths in the upper part of the thoracic oesophagus. If the patient is reasonably fit the reconstruction of choice is probably a cervical oesophago-gastric anastomosis, but this operation is of such severity that many patients are unfit to withstand it; in these cases a palliative procedure is indicated.

Palliative Procedures

Inoperability Decided Before Operation.—If the growth is situated in one of the less favourable positions, such as the upper thoracic portion of the oesophagus or at the upper

thoracic outlet, and if in addition the patient is a poor surgical risk, it may be unwise to attempt any radical operation. In these circumstances the introduction of Souttar's tube provides a good form of palliative treatment. The implantation of radon seeds through the oesophagoscope is practised successfully by V. E. Negus as a better form of palliation, but the technical difficulties and the special instruments necessary make this method unsuitable for all but the few. Simple palliation may be justified in certain cases, and, if combined with the swallowing of hydrogen peroxide solution, may enable the swallowing of soft foods to be resumed, but this method is not free from the danger of perforation of the gullet.

Inoperability Decided At Operation.—If an extensive surgical approach has been made and the condition is then found to be inoperable, every attempt should be made to carry out some palliative procedure which will enable the patient to regain the power of swallowing. For growths at the cardia, the best method of achieving this is by constructing a Roux loop en-Y and anastomosing it to the oesophagus, which is divided above the growth. For growths higher up in the thoracic oesophagus the best form of palliative short-circuit is to make use of the stomach. The whole of the stomach is mobilized and also that part of the oesophagus which lies below the level of the growth. The oesophagus is now divided above the growth, the lower end securely closed, and the upper cut end anastomosed to the fundus of the stomach, which, if necessary, can be brought above the arch of the aorta.

Post-operative Management

The patient is returned from the theatre with a drainage-tube connected to an under-water seal, and the tube is usually removed after four or five days. During the extraction of the tube care is exercised to prevent the entry of air into the chest. A daily examination of the patient's chest is carried out and a routine *x*-ray film is taken on the first, third, and seventh days. Aspiration of the chest is performed at the upper limit of the area of dullness elicited on percussion if the patient's respiration becomes embarrassed, or if more than one-third of the pleural cavity is seen to be occupied by fluid.

Resuscitation is aided in the immediate post-operative period by raising the end of the bed on blocks, placing the patient in an oxygen tent, and giving transfusions of blood, saline, or 5% dextrose as required. The drip is discontinued after 48 hours, and we find the patients can be sufficiently hydrated with oral and rectal fluid. Water containing 100,000 units of penicillin in 2 ml. is given in that dose every hour from the 12th to the 48th hour after the operation. On the third day 1 oz. (28 ml.) of half-strength saline or weak tea is allowed hourly, and on the fourth day 2 oz. (57 ml.) of this saline or citrated milk or tea is given hourly. Milk puddings, mashed potatoes and gravy, coddled egg, and thin bread-and-butter may be started on the sixth day.

The patients are usually undernourished and have little subcutaneous tissue, so that care must be taken to avoid the occurrence of bedsores. Careful supervision of the water seal is essential in order to prevent air entering the chest.

A careful watch is made every day, before and after operation, for the presence of thrombosis in the veins of the lower extremity.

If leakage occurs at the anastomosis, oral administration of fluids should be stopped, intravenous therapy reinstituted, and the drainage tube left *in situ*. One of our patients developed an ileus, and we were unable to pass a tube through the region of the anastomosis to decompress the intestine; we were eventually compelled to perform a blind jejunostomy for drainage. After decompression the patient fully recovered, swallowing was resumed without difficulty, and the jejunal opening closed spontaneously.

Regurgitation of acid gastric contents may occur after oesophageal operations. This regurgitation is painful and takes place after eating or when the patient lies down. It can be successfully treated by advising the patient to sleep well propped up, and by prescribing olive oil before meals and magnesium trisilicate after them.

Pathology

Most of the growths were squamous carcinomata (see Table III), nine were adenocarcinomata, and the rest were of the undifferentiated variety. One patient may have had two primary growths of the oesophagus. He was a man aged 64 with a six-months history of dysphagia, regurgitation, and weakness. The summary of the pathological report is as follows: "One ulcerating growth was situated in the region of the tracheal bifurcation; histologically it was seen to be a well-differentiated squamous carcinoma. The second lesion had not ulcerated, and was 2 in. (5 cm.) above the cardia. Histologically an anaplastic spheroidal cell growth with no evidence of squamous origin was observed, the cells of which were rather loosely arranged on a firm connective-tissue strand suggesting papillary arrangement. It appeared to be a separate tumour and not a metastasis of a squamous carcinoma."

TABLE III.—*Histology of Growth*

Squamous carcinomata	67
Undifferentiated squamous carcinomata or anaplastic growths	16
Adenocarcinomata	9

Two patients had the type of growth which spreads extensively under the mucosa of the oesophagus.

Complications

Pulmonary complications (see Table IV) are still the major problem following the radical operation, although the lungs are inflated during and at the termination of the operation. The use of sulphonamides and antibiotics has decreased the incidence of these complications but has not abolished them.

TABLE IV.—*Complications Causing Death After Operation*

Causes of Death	No. of Patients
Pulmonary collapse or congestion	7
Pulmonary infarction	1
Leakage of anastomosis	2
Peritonitis	1
Internal strangulation	1
Cerebral arteriosclerosis	1
Unknown	1

Early in 1947 a fatal herniation occurred through the diaphragm alongside the mobilized bowel.

Leakage at the anastomosis has occurred twice in this series, excessive mobilization presumably having imperilled the blood supply.

Results (See Table V)

It is difficult to find in the literature any considerable series of cases of carcinoma of the oesophagus accompanied by the enumerations of long-term survival. The experiences of Sweet and Garlock are exceptions to this, and so far as we have been able to ascertain their figures have been unsurpassed.

TABLE V.—*Treatment and Results of the Last 72 Patients*

Treatment	No. of Patients	Lived 1–28 Days	Lived 1–6 Months	Lived 6–24 Months	Living
Resections	29	15	6	3	5
Palliative operations	8	5	—	3	—
Explorations	5	3	1	1	—
Jejunostomy	15	6	7	2	—
Gastrostomy	13	3	5	4	1
No treatment	2	2	—	—	—

The longest survival in the present series following resection of the growth is that of a woman aged 57, who has now lived, with no clinical evidence of recurrence, for over

four years. She complained of heartburn after operation, but this was successfully treated by alkalis. She swallows without difficulty and has continued her work as a housewife.

Two patients continue to thrive two years after operation; one of them, a woman, is now 69. Two other patients have survived for over 18 months—both had a carcinoma situated in the middle third of the oesophagus.

Of the 72 cases of carcinoma of the oesophagus at various sites 29 had resections, and in 14 the patient survived longer than a month, giving a mortality rate of 51%. Supra-aortic anastomoses had been performed on 7 of the 15 patients who died within the month. The resectability rate was 40%. Eight palliative operations were performed, and three of these patients lived longer than six months.

Jejunostomy was performed on 15 patients and gastrostomy on 13; 7 of these 28 patients have lived longer than six months. No patient in the total series who was not treated by radical operation has lived longer than two years.

Summary

An analysis of the various clinical features observed in 159 patients suffering from carcinoma of the oesophagus has been made. Cases of carcinoma arising in the stomach and involving the oesophagus have been excluded.

Of the investigations, oesophagoscopy is the more exact method of obtaining correct information about the presence or absence of a growth in the gullet. Repetition of a barium swallow may at times be necessary to avoid missing the presence of a small growth.

The use of concentrated liquid food facilitates the preparation of the patient to withstand the severe radical or less severe palliative procedures. With radical treatment, although the mortality is high (50% approximately), the patient may be returned to a normal state with the ability to swallow restored.

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The *Hungarian News and Information Service* in London, the official mouthpiece of the Hungarian Government, has lately issued several announcements on medicine and science in that country. On March 15, 83 Kossuth Awards were presented at a ceremony in the House of Parliament at Budapest. Kossuth was the leader of the 1848 Hungarian revolution, and these national awards were instituted on the centenary of its outbreak, and are since given annually for outstanding work in the arts, sciences, industry, and agriculture. In the medical section this year Professor György Ivanovits received 10,000 forints for the isolation of vitamin B_{12}, Professor Ferenc Kiss a similar sum for research on the vegetative nervous system and the lymphatics, and Professor Imre Töro 20,000 forints for the discovery of a new mechanism of cell division. According to a report by the secretary-general of the Academy of Sciences there will be 25 scientific congresses in Hungary during the year, to which 200 foreign guests will be invited. In May there will be a medical congress on the work of Sándor Korányi (1866–1944), a specialist on traumatic diseases. A new Hungarian Biological Association was founded on March 30 at a meeting at the Academy of Sciences. Professor Sándor Jávorka, who received a 1952 Kossuth prize for his studies on the Hungarian flora, was chosen as president, and István Boros, director of the National Science Museum, as secretary.

CANCER OF THE HYPOPHARYNX AND ITS SURGICAL TREATMENT

BY

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Cancer in any part of the pharynx is a serious disease, for it causes severe suffering and is attended by a high mortality. In the hypopharynx these effects are maximal because of gross interference with respiration and deglutition, and the number of patients who have been cured is small. Thus any form of treatment that will relieve the patient's suffering, and is also designed to effect a cure, is welcomed. Contemplation of the serious plight of patients with this disease stimulated me several years ago to study the surgical problems involved in the radical extirpation of the hypopharynx and its lymphatic drainage, and I studied the work of Trotter (1929, 1932), Colledge (1940–3), and Wookey (1948) with profit. In addition, by the clinical examination of patients and a study of pathological specimens and necropsy reports, I sought a better understanding of the behaviour of the disease.

The object of this paper is to present some of my experiences in the treatment by radical surgical operation of a series of 18 patients with cancer of the hypopharynx. Most of them were suffering from advanced disease; some had been pronounced untreatable, were in a sad plight with dyspnoea, stridor, or dysphagia, and had been sent home to await their end. Others had received radiotherapy, but the disease was extending. One patient had had a tracheotomy, with severe dermatitis of the skin of the neck and anterior chest wall; another patient had had a gastrostomy. Their ages varied from 38 to 75, and many were in a very poor general condition.

Classification and Spread of the Disease

Trotter delineated the following areas as the origin of the disease: the epiglottis, glosso-epiglottic fold, aryepiglottic fold, pyriform fossa, posterior wall, and the post-cricoid region. In many patients I was unable to determine the site of origin owing to the large area of the hypopharynx which was involved, even from the pharyngo-oesophageal junction to the oropharynx. In some patients the disease is of multicentric origin, and malignant foci are present in several parts of the hypopharynx and larynx. The growth possesses a high degree of malignancy and is usually a squamous-cell ulcerating lesion. From its origin the disease spreads as shown in Table I.

TABLE I.—*Cancer of the Hypopharynx: Methods of Spread*

Direct extension	Pharynx, oesophagus, pharyngo-laryngeal septum, larynx, trachea, thyroid gland, internal jugular vein, pre-vertebral fascia, cervical vertebrae, skin.
Lymphatic metastases	Deep cervical, para-oesophageal, and superior mediastinal lymph nodes.
Haematogenous metastases ..	Lungs, liver.

When the growth is localized to one-half of the hypopharynx the deep cervical lymph nodes on the same side are often involved, but those on the opposite side may also be affected. If the growth passes across the midline the lymph nodes on both sides may be the site of metastases. Consequently in every patient I advise a block dissection of the

lymph nodes on both sides of the neck, but I leave the internal jugular vein and the sterno-mastoid muscle on the side where the lymph nodes are smaller.

Early Symptoms and Signs

These are often vague and the patient is unable to describe them accurately. There may be the sensation of a foreign body in the pharynx and a constant desire to clear the throat. Thickness of the voice develops and discomfort with swallowing occurs. As the disease progresses definite symptoms are experienced; these include dysphagia, dyspnoea, voice hoarseness, and a periodic cough. Patients sometimes come with a lump in the neck caused by lymphatic metastases, or severe pain in the ear, which is worse when swallowing occurs. The symptoms also vary according to the site affected. Thus, post-cricoid carcinoma affects women of a younger age group than men with the disease in other parts of the pharynx. In these patients dysphagia of various degrees is present for a number of years and becomes worse when malignancy develops. Minimal symptoms are usually caused by a growth in the posterior wall, and lymph-node metastases are often present when the patient is first seen. When the lateral wall and arytenoid regions are involved marked oedema develops which causes dyspnoea and voice hoarseness. In the clinical examination special attention is given to the neck for enlarged lymph nodes, and deviation, thickening, widening, and fixation of the pharynx and larynx. When dyspnoea and stridor are absent the hypopharynx and larynx are examined by the indirect and direct inspection methods, biopsy is performed, and the general condition of these organs is noted.

Radiological examination may give additional information regarding the site and extent of the lesion. Thus a soft-tissue shadow is seen in a plain *x*-ray film of the neck; tomograms and a barium swallow are also done.

The Problem of Stridor, Dyspnoea, Asphyxia, and Dysphagia

Several of my patients had severe respiratory obstruction caused by an extensive growth and surrounding oedema. Before the radical operation a tracheotomy must be avoided if possible, as this causes a number of technical difficulties. Nothing, therefore, is done in the pre-operative period to exacerbate the pharyngo-laryngeal oedema, and I defer direct pharyngoscopy and laryngoscopy in these cases until the patient is in the operation theatre for the major operation, when biopsy and histological examination are performed with the frozen-section technique. On several occasions, because of severe dyspnoea, even the extraction of carious teeth has been deferred until some time after the major operation. Sometimes, as the first step in the major operation, I have instituted a tracheotomy for almost complete respiratory obstruction under local infiltration analgesia with procaine hydrochloride (strength 1%). The remaining steps of the operation are then completed under endotracheal anaesthesia.

When the carcinoma involves the pharyngo-oesophageal junction complete dysphagia may be experienced. If this has been present for several days before the patient is seen, a gastrostomy may be required so that the general condition can be improved before the radical operation is performed. When, despite severe dysphagia, the patient's condition remains satisfactory, intravenous feeding is carried out and a gastrostomy is avoided. If a temporary gastrostomy is required it is allowed to close when the patient is able to swallow normally.

Principles of Radical Pharyngeal Surgery

A radical operation for cancer includes the removal of the affected organ with any malignant extensions to the neighbouring tissues and the regional lymph nodes as a monoblock dissection. In addition to the clinical and special examinations carried out, an exploration of the neck is required to determine the operability of the lesion and the extent of the resection which is required to eradicate the disease.

Laryngo-pharyngectomy and Laryngo-oesophago-pharyngectomy

These operations, combined with a bilateral lymph-node block dissection, fulfil the above conditions satisfactorily. The former operation is done when the growth is in the upper part of the hypopharynx involving the epiglottis and glosso-epiglottic and aryepiglottic folds. The latter operation is performed when it is in the lower part, such as the pyriform fossa or post-cricoid region. For the higher growths it is necessary to divide the pharynx above the level of the hyoid bone, which is included in the resection. When the growth is localized and low the cervical oesophagus is divided at the thoracic inlet and the hypopharynx below the hyoid bone. The lateral lines of excision lie posteriorly to both carotid sheaths, so that the cervical lymph nodes and cellular tissues are included in the block of tissue removed. The internal jugular vein and sterno-mastoid muscle are excised on the side where the lymph nodes are more extensively involved.

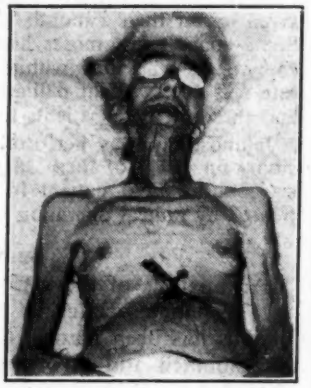

FIG. 1.—Clinical photograph of a woman aged 67 with a gastrostomy for complete dysphagia due to an extensive post-cricoid carcinoma invading the cervical oesophagus.

The Two-stage Operation.—The excisional stage of the operation having been completed, the patient is left with a temporary lateral pharyngeal fistula through which a rubber feeding-tube is passed into the upper opening of the oesophagus and on into the stomach. After an interval of four to six weeks a reconstruction procedure is performed to re-establish normal deglutition. This is achieved by making a new hypopharynx from the skin of the neck and anastomosing it to the oropharynx above and to the oesophagus below. This new pharynx is placed in the normal anatomical position of the organ and is covered by a rotation skin flap from the neck or by a tubed-pedicle skin graft from the acromio-pectoral region. I have performed this operation in the majority of my patients.

FIG. 2.—Clinical photograph of the same patient as in Fig. 1 after laryngo-oesophago-pharyngectomy (two-stage operation); she is alive and well 34 months later and swallows normally.

The One-stage Operation with Primary Closure.—When conditions are favourable an end-to-end anastomosis can be made between the upper segment of the divided hypopharynx and the pharyngo-oesophageal junction, with primary closure of the neck. I performed this operation for a patient with a localized carcinoma in the right pyriform fossa and metastases in the right upper deep cervical lymph nodes. The procedure was

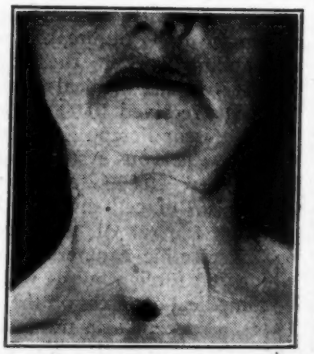

FIG. 3.—Clinical photograph of a woman aged 61 after laryngo-oesophago-pharyngectomy (two-stage operation) for a post-cricoid carcinoma; she is alive and well 12 months later and swallows normally.

facilitated by a severe fixed kyphosis of the cervical vertebrae, so that the divided ends could be brought into apposition without tension, and the connective tissues in the submaxillary region were reflected down to cover the anastomosis. The wound healed well and the patient was swallowing perfectly five weeks after the operation. He remains well 15 months later.

Pharyngectomy with Conservation of the Larynx.—It is a temptation to conserve the larynx when the carcinoma in the hypopharynx is relatively small. Thus for an early carcinoma in the pyriform fossa I have performed a partial pharyngectomy with reconstruction of the pharynx as a one-stage operation. In another patient with a post-cricoid carcinoma the entire hypopharynx was removed with the construction of a new skin pharynx.

Laryngo-partial Pharyngectomy.—In this operation a strip of the posterior pharyngeal wall is conserved, the patient being left with a median pharyngeal stoma. This is a great advantage in patients who have had a full course of irradiation and in whom degenerative changes have occurred in the skin and other tissues of the neck, rendering the construction of a new skin pharynx very difficult. The resources of the surgeon may be severely taxed in finding ways to solve these problems. I have found the formation of this stoma, with subsequent closure by hinged flaps and acromio-pectoral tubed pedicle flaps, a great help.

Choice of Operation

From my experience I feel that the best operations for cancer of the hypopharynx are laryngo-pharyngectomy and laryngo-oesophago-pharyngectomy, with removal of the cervical lymph nodes on both sides as a monoblock procedure. These should be carried out even when the primary growth is relatively localized, as they give the patient the best chance of a cure. Operations with conservation of the larynx are not nearly so satisfactory as regards function and the possibility of recurrence. For example, one patient who had a partial pharyngectomy for a carcinoma in the pyriform fossa developed metastases in the upper deep cervical lymph nodes on the opposite side two years later; another patient who had a resection of the hypopharynx and conservation of the larynx died from local recurrence one year later.

End-results of Operation

The present series comprised 18 patients with a squamous-cell carcinoma of the hypopharynx, proved by microscopical examination. In 14 the disease was very extensive in the pharynx; in some it extended into the oesophagus, larynx, or surrounding tissues in the neck. In nine metastases were proved microscopically in the cervical lymph nodes. Irradiation treatment had been given to four patients before surgery was undertaken for progressive disease. There was no operative mortality. The end-results with all types of operation are set out in Table II; it is realized that the patients must be followed up for a much longer period of time to get the final assessment.

TABLE II.—*End-results with All Types of Operation*

	Period in Months after Operation
10 patients alive	2 11 12 12 14 15 15 24 25 34
6 patients died of cancer ..	4 8 12 12 23 23
2 patients died of other cause	2 10

Laryngo-pharyngectomy and Laryngo-oesophago-pharyngectomy.—Twelve patients have undergone laryngo-oesophago-pharyngectomy and four laryngo-pharyngectomy (in three a portion of the pharyngeal wall was conserved, and in one an end-to-end anastomosis was done); the end-results are shown in Table II, which includes two patients who survived 12 and 23 months respectively after undergoing pharyngectomy with conservation of the larynx.

When the results of surgery are considered the condition of the patients after operation must be taken into account in addition to the survival periods. Operation brings relief from the distress of dyspnoea, stridor, and dysphagia; a gastrostomy is allowed to close, and a palliative tracheotomy with surrounding infection and dermatitis is converted into a well-managed tracheostomy. The patients are enabled to swallow normally all types of food, can wear ordinary clothes, and live happy useful lives. Voice production is variable, but not so good as after laryngectomy. A number of the men can return to work. A good example is that of a man with severe stridor who was considered elsewhere to be in a hopeless condition and who is now back at work. One female patient married for the second time after the operation, and another woman, aged 67, who had had a gastrostomy performed elsewhere for severe dysphagia, is well and swallowing normally 34 months later, and the gastrostomy has closed. None of my patients have developed a fibrous stricture at the junction of the new skin pharynx and oesophagus, or elsewhere.

Pharyngectomy with Conservation of the Larynx.—Two patients underwent this operation. One patient with a carcinoma of the left pyriform fossa had a partial pharyngectomy with a block dissection of the lymph nodes in the left side of the neck. She spoke and swallowed normally until metastases developed in the right upper deep cervical lymph nodes and she died 23 months later. The other patient had a post-cricoid carcinoma, and she requested that her larynx should be preserved. Total excision of the hypopharynx was performed with the construction of a new skin pharynx as a two-stage operation. The functional result was bad, as fluid entered the larynx on swallowing, so a gastrostomy was necessary. The patient died one year later from a recurrence in the neck.

Summary

An account is presented of some of my experiences in the radical surgical treatment of a series of 18 patients with carcinoma of the hypopharynx. Most of the patients had advanced disease and were suffering severely.

It is shown that radical surgery has an important place in the treatment, for distressing symptoms are relieved and there is the possibility of cure.

I believe the best operations are laryngo-pharyngectomy and laryngo-oesophago-pharyngectomy with a bilateral block dissection of lymph nodes as either one-stage or two-stage procedures.

Radical surgery can be undertaken also when irradiation has failed to control the disease. Patients live happy useful lives after the operation.

The length of survival is presented, and it is hoped time will prove that a number of them have received permanent benefit.

I have had the valuable co-operation of Dr. L. H. Morris and Dr. A. Chester in the anaesthesia of the patients; my registrars, house-surgeons, and the nursing staff have helped in every possible way, and I wish to thank them all. Portland Plastics Ltd. kindly supplied me with "polythene" tubing for use in my work.

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The U.S. Army Medical Service has decided to accept medical students as interns in Army hospitals immediately they qualify. This new scheme will start on July 1, when 146 senior medical students representing 51 medical schools will, provided they pass their examinations, be commissioned as first lieutenants in the Medical Corps Reserve and go to one of 10 Army teaching hospitals in the U.S. or to Tripler Army Hospital, Hawaii.

A NOTE ON THE ABSOLUTE VIABILITY IN WATER OF S. TYPHI AND THE DYSENTERY BACILLI

BY

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AND

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The genesis of this minor investigation was an inquiry by a clinical colleague about the maximal survival times of the dysentery bacilli in water. Our failure to find any precise figures for these times in the reference works that we consulted led us to make the following experiments.

Experimental Tests

Suspensions of *Salmonella typhi, Shigella sonnei, Shigella flexneri* Y, and *Shigella shigae,* each at a concentration of 1,000 million organisms per ml.—measured by opacity standards—were made in tap-water, in distilled water, and in normal saline. Ten-millilitre volumes of each of these suspensions were then kept in diffuse daylight at room temperature under aerobic conditions, and were tested for viability by the removal, at regular intervals, of a standard loopful of each suspension, which was inoculated into a tube of glucose nutrient broth. The loop employed was one of 4-mm. diameter. These transplants were incubated at 37° C. and their growth was confirmed, and checked for purity, by plating on MacConkey's agar. The plate cultures were then identified by their sugar-fermentation tests and their agglutination reactions with standard sera. If no growth was obtained from the loop transplant, 1 ml. of the suspension was withdrawn in a sterile pipette and inoculated into a fresh tube of glucose nutrient broth, which was incubated for 72 hours at 37° C. and then plated on MacConkey's agar, before the suspension was discarded as non-viable. Temperature readings were taken daily of the small room in which the suspensions were kept. The minimum temperature recorded was 45° F. (7.2° C.) and the maximum 95° F. (35° C.), giving a mean over the whole period of the experiments of 70° F. (21.1° C.).

The suspensions had evaporated to approximately half their original volume after 90 days, and to dryness after 236 days, and no growth was obtained from any of them after the addition of glucose nutrient broth to the dried residue. Before this occurred the following observations had been recorded, the figures in Table I representing the particular length of time in days.

TABLE I

	Tap Water		Distilled Water		Normal Saline	
	Viable	Dead	Viable	Dead	Viable	Dead
Salm. typhi ..	211	236	211	236	153	188
Sh. sonnei ..	68	86	211	236	153	188
Sh. flexneri Y ..	86	118	118	153	118	153
Sh. shigae ..	2	8	2	8	68	86

As this experiment was vitiated to some extent by the evaporation of the suspensions to dryness before the presumptive death of the organism in three instances, a second experiment was performed under the same storage and test conditions. Two suspensions of each organism were made in distilled water to a volume in each case of 200 ml. One of these (A) had a concentration of 500 million organisms per ml.; the other (B) had a concentration of 1,000 million organisms per ml. The readings are given in Table II.

TABLE II

	A		B	
	Viable	Dead	Viable	Dead
Salm. typhi ..	24	59	443	474
Sh. sonnei ..	82	107	168	197
Sh. flexneri Y ..	197	238	364	391
Sh. shigae ..	2	7	2	7

Conclusions

It would seem, from these observations, that an important factor in the absolute viability of *Salm. typhi, Sh. sonnei,* and *Sh. flexneri* Y in a chemically inert medium, such as distilled water, is the size of the cell population, at any rate up to a larger population than we have tested.

We offer no explanation of our inconsistent readings with *Sh. sonnei* and *Sh. flexneri* Y, we merely record them; but they suggest that the problem of the absolute viability of bacteria in water is a complex one that is worthy of a more profound study than we have attempted.

The strains of the four bacteria used in this study were obtained from the National Collection of Type Cultures.

A CASE OF MYOSITIS OSSIFICANS PROGRESSIVA

BY

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Myositis ossificans progressiva is a rare congenital disorder producing progressive crippling in childhood and adolescence. The subject has been reviewed by Mair (1932) and more recently by Fairbank (1950), who recorded two further cases.

This report adds another case to the literature and illustrates the characteristic course of the disease and the distressing immobility to which the patient is reduced.

Case Report

This patient, a woman now aged 24, the youngest of five children and the only member of the family to suffer from this or any relevant disease or abnormality, was normal at birth, and for three years after was in excellent health. At the age of 3 she fell while playing and injured the left side of her neck. The next day a painful red lump developed in the region of the left sterno-mastoid muscle. A week later, and without further trauma, she developed a similar mass in the left mastoid area. This was thought to be mastoiditis, and as such was submitted to operation, but no pus was found. There was no aural discharge.

Later, numerous other masses developed in the muscles of the back and arms. Some of these were likened to "bunches of grapes." As the swellings disappeared the spine was left rigid and the arms remained extended.

At the age of 7 she was quite unable to bring her hands to her mouth to feed herself, but gradually the elbows flexed, allowing a restricted range of movement, so that by the age of 9 she could feed herself, could comb her hair, and could walk without assistance.

When 11 she fell on to her left knee. This became red, tender, and swollen, and this condition persisted for six weeks. As the swelling dispersed the knee became ankylosed and has remained so. Three years later her left hip became painful and ankylosis developed. As her right knee and hip were still mobile she was able to walk, and she worked as a telephonist.

FIG. 1.—A support is essential to enable her to stand.

The right knee also became ankylosed after an injury when she was 16, and the right hip fused soon after. She could now only totter after being assisted into the erect position. At this time she had a painful exostosis of the right os calcis; this was excised, leaving a normal scar. Pain and swelling occurred in the right elbow when she was 19 and complete ankylosis ensued. The same year she was admitted to Tilbury Hospital, and appendicectomy was performed for subacute recurrent appendicitis. Recovery was uneventful, and a normal scar remains. At the age of 20 she was admitted to another hospital and the left biceps muscle was excised with the aim of mobilizing the elbow, but this was not successful. Histological examination of the muscle failed to reveal any abnormality.

The left elbow has fused recently after an attack which involved the wrist and finger flexors.

From the age of 3 to 24 there have been many acute episodes which have consisted of severe aching pain, with inflammatory-like swellings. While some were related to minor trauma, most developed spontaneously, unassociated with any known cause. Their duration was from a week to several months, and most of them left residual stiffness and new bone formation, though after some the patient reverted apparently to her previous degree of disability.

Menstruation began at 14 and was regular until 17, when her periods became scanty; they are now absent.

In March, 1950, a portion of ectopic bone was removed from the right buttock and was found to be lying in the subcutaneous fat (see biopsy report). This was followed by a course of radiotherapy to the right buttock. No further bone deposit has appeared in this site.

An arthroplasty of the right elbow was performed to enable the patient to feed herself, but this was followed by new bone formation and the return of ankylosis.

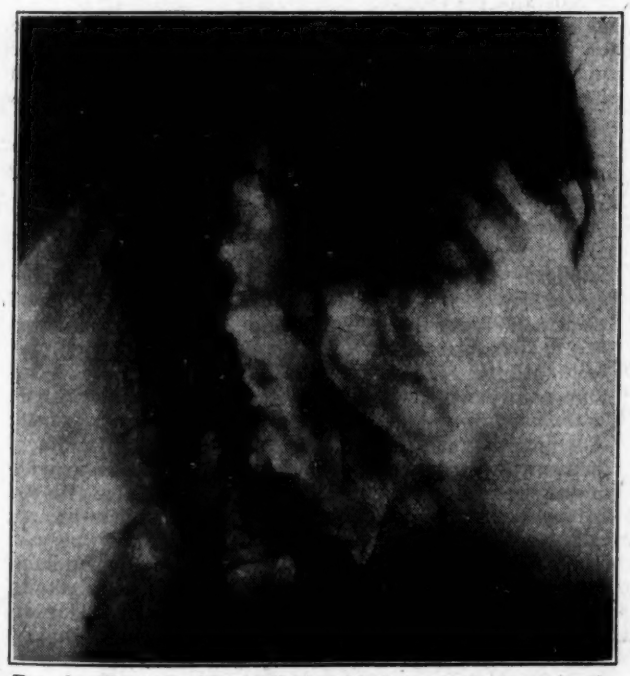

FIG. 2.—Fixed lumbar scoliosis with heterotopic bone in the muscles of the chest and trunk.

FIG. 3.—There is complete ankylosis of the cervical spine.

On examination the patient was seen to be a slim, cheerful young woman completely rigid from skull to ankles. She was quite unable to walk and could stand only after being propped against a wall or supported by a pole (see Fig. 1). She was 5 ft. 6 in. (168 cm.) in height and weighed 7 st. (44.5 kg.). Her skin was greasy from seborrhoea oleosa. Excessive hair was present on her limbs, and her breasts were small.

She had ankylosis of the whole spine and of all the large limb joints (shoulders, elbows, hips, and knees). There was a marked lumbar scoliosis, convex to right, with the pelvis raised on the left side (see Figs. 2 and 3). The shoulders were held in adduction and internal rotation. Both elbows were acutely flexed. The lower limbs were rigidly extended with the knees in contact. Some movement was present in both ankles and temporo-mandibular joints. The left ankle lay in equinus, while the right was in the neutral position. The jaw opened to a width of ¾ in. (1.9 cm.) between the teeth. There was a full range of movement of the joints of the hands and feet, though the radiocarpal movements were from 20 degrees flexion to 90 degrees extension, with gross radial deviation. Large bony-hard masses protruded irregularly over the back on each side of the spine and extended laterally to the upper limbs and to many other parts of the body, including the lower limbs and the right temporalis muscle (see Fig. 4). There were exostoses of the left fifth metatarsal bone and of the right talus, which had ulcerated through the skin. A recently developed indurated mass was seen on the anterior aspect of the left forearm, involving the flexors of the fingers. This had produced a flexion contracture of the middle finger, which could be extended only by flexing the wrist. There was bilateral hallux rigidus, but no valgus, microdactyly, or other

FIG. 4. — Diagram showing sites of new bone formation.

abnormality (Mair, 1932). The upper thoracic cage was rigidly fixed, while the lower ribs moved on respiration. The abdomen was normally supple, and the appendicectomy scar well healed.

A biopsy report on June 19, 1950, stated: "The specimen is dense smooth white bone 2.2 by 2 by 1 cm., seen on section to consist of well-formed cortical lamellar bone, traversed by Haversian systems, and also central trabeculae of lamellar spongy bone enclosing adipose marrow." Extensive laboratory tests gave no abnormal values.

A radiological report stated: "There is widespread deposition of extraskeletal bone, particularly around the shoulder- and hip-joints and on each side of the vertebral column. The asymmetrical arrangement of bony bands has caused scoliosis.

Discussion

This disease is characterized by the deposit of heterotopic bone in relation to voluntary muscle. Although muscle groups appear to be involved it seems certain from the literature that the fibrous layers of fascia and aponeuroses are the primary sites, and that the process spreads into the adjacent muscle, where new bone forms (Greig, 1931). This patient illustrates many of the characteristic features. The onset within the first two years of life is common, though it has been known to begin in adults (Frejka, 1929) and to have been present at birth (Mair, 1932). The absence of anything similar in the family history is in keeping with most recorded cases, though Burton-Fanning (1901) calls attention to a father and son who were victims of the disease. It is estimated that in 75% of cases there is an associated abnormality of the hands or feet—for example, microdactyly or hallux valgus (Ryan, 1945). In this case no such malformation was present. These concomitant congenital lesions, which suggest that the origin of the disease is prenatal, are sometimes inherited (Rosenstirn, 1918).

Laboratory tests and the bone biopsy failed to reveal any abnormality. The bone appears to arise in connective tissue where haemorrhage has occurred.

While most patients are boys, no significance can be attached to this, for in a rare disease the sex ratio may well be distorted. No relationship was discovered to infection or "rheumatism." Trauma plays a varying part in the production of episodes. It may determine the location of the lesion or may be noticed and be given exaggerated importance in the initial stage of the episode.

The effect of excising a prominent piece of bone in the back and following with a course of deep *x*-ray therapy (1,000 r) has been tried. So far as can be determined, no new bone has formed at this site. It is improbable that radiotherapy will improve the surgical efforts, till now disappointing, to mobilize joints. No method of treatment has yet been found to have any effect on the progress of this condition, which pursues a relentless course until the whole body has been immobilized, and finally the patient succumbs to intercurrent infection.

I am indebted to Dr. I. Doniach for the pathological report, to Miss H. Wilson for Fig. 4, and to Mr. M. R. Ewing for permission to publish this case.

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In London on May 7, 8, and 9 is being held the first International Home Help Conference, at which, under the auspices of the National Association of Home Help Organizers, delegates from comparable organizations in Belgium, Finland, France, Holland, Norway, Sweden, Switzerland, and other countries will discuss administrative problems in this branch of social welfare.

A CASE OF GLANDULAR FEVER WITH CEREBRAL COMPLICATIONS

BY

I. M. LIBRACH, M.B., D.P.H., D.C.H.

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Crowther (1951) described the case of a man aged 20 with glandular fever and involvement of the central nervous system, and summarized reported cases. Because of their paucity another is recorded.

Case Record

An unmarried seamstress aged 19 was admitted on August 21, 1951. Three weeks previously, while camping, she complained of persistent headache and giddiness. Seven days before admission the giddiness worsened, especially on looking to the left, objects rotating clockwise. She complained of intense malaise and pain in the back. She noticed that speech and thinking were difficult. For 48 hours before admission she was nauseated and vomited several times. Micturition was normal, the bowels were costive, and menstruation was normal. Her past history was uneventful.

On examination she was apyrexial; pulse rate 64, regular: respirations 22. She was a well-built girl with a vacant expression, drowsy, with thick speech, slow cerebration, and lack of concentration, although she answered questions rationally. There was no jaundice or anaemia; the lymph nodes were not enlarged. Neurological examination showed diminished deep reflexes in the arms and legs; abdominal reflexes were present; plantar reflexes were flexor. There was no sensory loss or paralysis. The pupils were unequal, the left being larger than the right; reaction to accommodation was brisk, sluggish to light. Retinoscopy was normal. Other systems were normal.

Drowsiness continued for four days, with some retention of urine, relieved by catheterization. She vomited bilious fluid several times and still complained of headache and giddiness, especially on moving the head. There was also considerable photophobia and she was content to lie listlessly in bed. Six days later the headache and giddiness were less severe, and she was rational, fully conscious, and orientated in time and space. Progress was uneventful, and she was discharged on September 8. Treatment was symptomatic.

When seen on September 25 and October 9 she had lost some weight, but looked and felt well. No abnormal physical signs were detected.

Investigations.—On admission, catheter-urine was normal; culture, sterile. Rectal and vaginal swabs contained no pathogens. The Widal test for enteric and abortus groups was negative. Blood urea, 34 mg. per 100 ml. White-cell count 7,800 (polymorphs 37%, lymphocytes 54%, monocytes 9%). Glandular fever cells present. Paul–Bunnell test, positive 1 in 512. Wassermann reaction and Kahn and gonococcal complement-fixation tests negative. On August 23 an *x*-ray film of the chest and skull was normal, and the Mantoux test negative at 1 in 1,000. On August 24, by lumbar puncture, 15 ml. of clear colourless fluid was withdrawn; pressure 100 mm. H_2O. There was a free rise and fall on jugular compression. Cerebrospinal fluid showed: cells less than 1 per c.mm.; protein, 25 mg. per 100 ml.; globulin, no increase; sugar, 75 mg. per 100 ml. Paul–Bunnell test negative. No organisms direct or on culture. On September 6 the Paul–Bunnell test was positive 1 in 256. On September 25 the Paul–Bunnell test was still positive 1 in 256. White-cell count was now 6,200 (polymorphs 45%, lymphocytes 45%, monocytes 9%, eosinophils 1%).

Discussion

This case raised several problems. Without fever or palpable lymph nodes and spleen it is probably impossible to diagnose glandular fever clinically. The history and signs suggested enteric fever or leptospirosis. Until the white-cell count was done the diagnosis was not suspected. No history of sore throat or swelling of the neck was admitted by the patient or her relatives. Because of her rapid recovery it must be assumed that she was in the late stage of the illness, any premonitory signs being overlooked—in contrast with Crowther's patient, who was desperately ill. As Tidy (1950) says, diagnosis is difficult in a patient who some time after a pyrexial attack presents with lymphocytosis, for either this or glandular swelling may persist for some months.

A surprising feature was the normal cerebrospinal fluid. This, however, is not incompatible with involvement of the brain substance, especially in virus disease. Greenfield (1947) holds that the diagnosis of encephalitis during life, especially in sporadic cases, depends more on elimination than on finding specific changes in the blood or cerebrospinal fluid. Many diseases may simulate encephalitis, and it may be impossible to make a definite clinical diagnosis.

The cerebral signs could be due to toxaemia from preceding generalized infection with the virus, if such be the cause of infectious mononucleosis. On the other hand, the normal cerebrospinal fluid could be accounted for by an acute toxic encephalopathy as distinct from meningitis (Brain, 1947).

The neurological manifestations of this disease, however, are varied and bizarre. There is no constant order in which the ordinary manifestations and the neurological symptoms develop, and they may vary in their comparative severity. They may occur simultaneously, as in the case of Epstein and Dameshek (1931), or at some interval after the systemic signs, as in Geliebter's (1946) and Crowther's (1951) cases; or the fever may have run its course, to be followed by nervous symptoms, or the latter may precede the former. Tidy (1950) says that in the more severe neurological forms the glandular swelling tends to be slight and may be overlooked.

The interpretation of the Paul-Bunnell reaction in neurological cases needs careful consideration, especially in the absence of other evidence. So far as is known, it is not positive in high titre in any other disease (Tidy, 1951, personal communication). In a disease with so bizarre a clinical picture, however, it is equally difficult to assess a negative reaction. Many missed cases or cases not diagnosed might have proved positive on repetition later in the disease.

Neurological involvement in a disease which essentially affects the reticulo-endothelial system is of puzzling interest. It may occur because the normal cerebrospinal fluid contains a varying number of lymphocytes and large monocytes, derived from the meninges and the brain tissue itself, and entering the cerebrospinal fluid via the perivascular spaces. Again, van Bogaert (1933) believes that post-infective encephalomyelitis is allergic in origin, and Rich (1946-7) has demonstrated the vascular basis of hypersensitivity. Miller (1951), too, has summarized the evidence, and thinks that the post-infective encephalomyelitis of measles, etc., polyarteritis nodosa, and cerebral serum sickness have a common allergic basis. He feels that the post-infective group is a manifestation of hypersensitivity to some antigenic product in a variety of infections chiefly of virus origin and acting selectively on the nervous system, just as glomerulonephritis is said to be due to streptococcal hypersensitivity.

The multiplicity of the nervous symptoms in glandular fever suggests, too, an allergic origin; for there is no known virus infection, apart possibly from poliomyelitis, which produces such capricious involvement at every level of the nervous system. In other words, the basic pathology of the nervous complications, or even of the disease itself, may be primarily a disorder of blood vessels—that is, an allergic vasculitis. Although antihistamine drugs were not used, it might be of interest to try their effect in future cases. Chloramphenicol has been tried, but in the absence of a known cause its use must remain empirical except in dealing with secondary invaders.

I wish to thank Dr. G. L. Brown, former medical superintendent, for his helpful criticism and for permission to publish, and to Mr. L. Whittaker, A.I.M.L.T., for the laboratory investigations.

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Medical Memoranda

Wandering Spleen During First Decade of Life

This is a comparatively rare condition. Most reports in the literature are confined to cases in which torsion has occurred. Abell (1933), in a review of the literature up to 1933, reported 95 cases with torsion. Emmett and Dreyfuss (1943) reported a further 25 cases between 1933 and 1943. At the Mayo Clinic only 2 out of 646 splenectomies performed prior to 1934 were for this condition.

The aetiology is that during the development of the stomach, when the dorsal wall rotates to the left it carries the greater omentum, in which the spleen develops, with it. If the attachments between the spleen and stomach are deficient the spleen gradually increases its range of movement (Truesdale and Freedman, 1938). Contributory factors are enlargement of the spleen and visceroptosis. In Abell's series torsion occurred most often between the ages of 20 and 40, with a preponderance of females but not a significant majority of multiparae. Only one case occurred in the first decade of life.

The case here reported is of interest in that it presented as an abdominal tumour and was first noticed by the parents of the child during the second year of its life.

Case Report

An African female child (Muzinza) aged about 10 was brought to hospital by her parents, as she had an abdominal tumour which they thought was gradually increasing in size. They were emphatic that they had first noticed the tumour on the right side when the girl began to walk during her second year. Living in a malarious area, they knew the normal position of an enlarged spleen. Apart from occasional fever, presumably malaria, the child had never been ill.

On examination she was seen to be rather thin and slightly anaemic. A visible protuberance was found to be caused by a tumour stretching from the umbilical to the right lumbar area. The tumour was smooth, firm, and painless even with movement. Repeated examinations of stool, urine, and blood showed no parasites. Her haemoglobin was 70% (Lovibond).

It was decided to perform an exploratory laparotomy. A lower right paramedian incision was made, this being the site of the tumour at the time. On incising the peritoneum the spleen presented and was readily delivered. Its attachments consisted of a grossly elongated pedicle and the omentum, which was adherent to the spleen in two places. The vessels in the omentum were very dilated, and it appeared as if a collateral circulation had been estab-

lished. No accessory spleen was felt. Splenectomy was performed. The spleen, which was of normal shape, weighed 280 g. The patient made an uninterrupted recovery.

My thanks are due to Dr. P. A. T. Sneath, late Director of Medical Services, Tanganyika, for permission to publish this article.

C. L. HALL, B.M., B.Ch.,
Medical Officer, Tanganyika.

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Trauma and Fibrosarcoma in the Foot

Fibrosarcoma in the extremities is uncommon: its occurrence in the foot is rare. Of the 24 cases of fibrosarcoma in the extremities collected by Bick (1938), only three were in the foot. In the present case the history of trauma is noteworthy.

CASE REPORT

A married woman aged 36 first attended hospital in April, 1946, complaining of pain and swelling of the first right toe, which had developed nine months previously, shortly after her husband had trodden on this foot. She also gave a history of having dropped a file on the foot two years earlier. Inspection showed the shape of the foot to be good, but there was a cystic swelling on the fibular side of the first toe, just distal to the metatarso-phalangeal joint. Movements of the joint were limited by pain. An *x*-ray film showed cystic spaces in the head of the first metatarsal, a satisfactory joint space, and complete degeneration of the head (see illustration). The patient was booked for "removal of the ganglion between the first and second right toes, with constructive removal of the head of the first metatarsal."

Radiograph of the fibrosarcoma.

One year later she attended hospital complaining of pain and swelling. This increased gradually, and in November, 1947 — 19 months after her first attendance — she reported that the pain had become "suddenly acutely severe," especially on the plantar aspect of the first toe. The swelling had markedly increased only in the preceding two or three weeks. She was admitted to hospital.

On examination the first right metatarso-phalangeal joint was swollen and there was a small cystic swelling in the first space, which was not fixed superficially, was probably not fixed to deep structures, and could be moved transversely only. It was tender to the touch, but not painful. The swelling appeared to extend along the first metatarsal. All movements at the metatarso-phalangeal joint were limited by severe pain. The blood Wassermann reaction was negative.

At operation a cystic swelling was found in the first space, white, tense, and elliptical—apparently of gelatinous consistence. It extended proximally along the fibular aspect of the first metatarsal and deeply into the foot. Only after removal of a considerable quantity was the extent of invasion appreciated, and no further exploration was undertaken. The capsule of the metatarso-phalangeal joint was completely absent, and the head of the metatarsal, while quite firm on its articular margin and apparently on its plantar aspect, showed trabeculation which produced cystic spaces. The mass of material seemed to be of capsular origin, and in appearance suggested myxoedematous degeneration. Part of the soft paper-like proximal phalanx was removed. The incision was closed, there having been much bleeding into the foot, and a firm bandage was applied. The report on the material from the foot was: "The main portion of the tissue is fibrous, but there are also areas with more or less densely packed small round or spindle cells advancing into the lymph spaces of the fibrous tissue. The appearance is that of a fibrosarcoma." Radiographs of spine and chest showed no metastases.

In view of the state of the foot revealed by operation, and the pathologist's report, an amputation was performed 7 in. (17.8 cm.) below the knee, and the patient was discharged a month later, apparently in good health, after measurement for an artificial limb. When last heard of, 45 months after operation, the patient was in good health.

COMMENT

It is accepted that the important predisposing factor in the development of carcinoma is chronic irritation, be it mechanical, repetitive, or chemical; and, despite one's acquaintance with the large number of injuries which do not end up with malignant change, sooner or later one is haunted by the part trauma appears to play in the development of sarcoma. In assessing the part played by trauma, it is helpful to bear in mind Walker's (1941) table: (1) Injury may cause disease. (2) Injury may precipitate disease. (3) Injury may aggravate disease. (4) Disease may promote injury (Ewing's "traumatic determinism"). (5) Injury may reveal disease. (6) The association may be pure coincidence. (7) In post-traumatic debility and invalidism sundry maladies and degenerations may be installed.

Sarcomata appear to follow a single injury, not always severe, and the features injury, persistent swelling, and/or haematomata, in the absence of fracture, are commonly found. The malignant degeneration usually takes place in the period of body growth, but not always. The striking feature to my mind is the story of an injury—to testicle, skull, limb, for example—causing temporary discomfort, which appears to begin to subside under whatever local treatment is given, but which, usually after a few weeks, rapidly becomes accentuated and the swelling more pronounced. Radical treatment at this stage does not usually succeed in preventing metastatic deposits. The absence of metastases is regarded as this particular patient's great and rare good fortune. The sequence of events, related so precisely by her, warrants the assumption that trauma played the decisive part in the development of her sarcoma.

Repair takes place by means of cell proliferation and by factors restoring function—presumably factors related to the part's function, affecting the differentiation of young cells—and the rate must similarly be controlled. Shaw (1935) notes that young cells of the proliferative stage of repair obtain their energy by glycolysis, whereas the differentiated cells obtain it by oxygenation from the blood stream. Thus, the early undifferentiated cell of repair resembles the cancerous growth in this respect. The view is advanced that, where function is unimpaired, stimulus to proliferation may result in malignant change—for example, (*a*) carcinomatous changes occurring in the sinus of chronic osteomyelitis; and (*b*) neoplastic change due to the long exposure of apparently healthy skin to tar preparations used in the repair of ulcers and to heal skin conditions.

As the character changes develop in only a minority of cases it must be assumed that other factors are also involved.

I wish to thank Mr. Rocyn Jones, of the Royal National Orthopaedic Hospital, London, for permission to publish this case, and Mr. David Trevor for his helpfulness and advice.

E. SILVERSTONE, L.R.C.P.&S.Ed.

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Reviews

THE SENSITIVE COLON

The Human Colon: An Experimental Study based on a Direct Observation of four Fistulous Subjects. By W. J. Grace, M.D., S. Wolf, M.D., and H. G. Wolff, M.D. Foreword by Alan Gregg, M.D. (Pp. 240; 112 illustrations, 31 in full colour. $7.50 or £2 10s.) New York: Paul B. Hoeber, Inc. London: William Heinemann. 1951.

This book will be studied with keen interest by all who have read *Human Gastric Function* by two of the present authors. The methods described for the study of the human colon are similar to those used in investigating gastric function in their well-known subject Tom. The greater part of the book records the results of a number of experimental studies in four patients with prolapse of the colon through the anterior abdominal wall. The colour, muscular activity, secretion, and mucosal fragility of the exposed portion of the colon were studied extensively under a variety of conditions. As in the previous work on the stomach, particular attention is paid to the changes produced by emotions, but the effects of a wide variety of drugs and of changes in temperature were also observed.

A chapter is devoted to changes in lysozyme secretion caused by emotions in both normal subjects and those suffering from ulcerative colitis, although the authors admit that there is no evidence that this enzyme can produce mucosal ulceration in the human being. The effects of vagotomy on the colon were studied in one subject in whom the operation did not appear to alter colonic function or improve the ulcerative colitis in any way. In another chapter 19 cases of ulcerative colitis are fully reviewed from the psychosomatic viewpoint, and improvement is said to have followed superficial psychotherapy in 13 of these.

The authors come to the conclusion that the colon reacts to emotions in a very similar manner to the stomach. Abject fear caused atony and blanching, whereas resentment, anger, and hostility caused contraction, hyperaemia, hypersecretion, and increased mucosal fragility. The effect of drugs followed the expected pattern, parasympathomimetic agents increasing blood-flow secretion and contractility, while sympathetic and ganglion-blocking agents had the reverse effect. But it was found that emotional stimuli would often produce greater effects than the drugs, leading to paradoxical results.

It may be objected that the number of observations and the criteria used are such that it is not justifiable to draw general conclusions from the subjects studied in this way, but this is to depreciate the ingenuity and energy with which the authors have set out to glean the maximum information from their necessarily limited material. They are studiously careful to separate their observations from their theories, and both will prove a stimulus to further research on the relation of emotional reactions to disease.

F. AVERY JONES.

FLOWERS AND FRUITS

The Quiet Art. A Doctor's Anthology. Compiled by Dr. Robert Coope. Foreword by W. Russell Brain. (Pp. 284. 12s. 6d.) Edinburgh and London: E. and S. Livingstone. 1952.

The Physician as a Man of Letters, Science, and Action. By Thomas Kirkpatrick Monro, M.D. Second edition. (Pp. 259. 21s.) Edinburgh and London: E. and S. Livingstone. 1951.

The first of these books is an anthology, mainly in prose, which relates to the practice of medicine. Dr. Coope has collected his quotations from hundreds of sources, ancient and modern, and made of them an inspiring and entertaining book. Sir Russell Brain in his introduction quotes the dictionary definition of an anthology as a collection of flowers, and for Dr. Coope's book this metaphor is just.

Dr. Monro's book is a *Who's Who* of doctors who achieved distinction (or notoriety) in fields other than medicine. Some of them, like Charles Darwin and Sydney Smith, early forsook the study of medicine; for others, like Keats and Goldsmith, medicine but temporarily confined their genius, while for some, like Linacre, Sydenham, and Osler, medicine remained their vocation and their glory.

Both books are in some degree complementary, and to browse through them together adds something of interest to each. Dr. Coope quotes Wilfred Trotter as saying, "You can always avoid the limelight if you try," and Dr. Monro records that in 1928 Trotter declined a royal honour. And if Dr. Monro does brief justice to the wittiest of Englishmen, Sydney Smith, Dr. Coope allows him thus to describe his hay-fever, "The membrane is so irritable that light, dust, contradiction, an absurd remark, the sight of a dissenter—anything sets me a-sneezing, and if I begin sneezing at twelve, I don't leave off till two o'clock—and am heard distinctly in Tarenton when the wind sets that way, at a distance of six miles."

Both these are bedside books to be read discreetly and intermittently. Both can induce the drowsy speculation which engenders sleep, but both will provide some essential homework for those who have the hardihood to deliver October addresses in the medical schools. Both give the reader some curious information. I learn from Dr. Monro that, while 71 doctors became sizable poets, no more than eight could be deemed artists. I learn, too, that it is more common to escape from medicine into crime than into the Church, and also that the profession can claim no more than seven distinguished sportsmen, including two brothers and one whist-player. And Dr. Coope tells us that John Mayou wrote in 1668 that "disease as it stalks through the land cannot keep pace with the incurable vice of scribbling about it." Many medical readers will find pleasure in these books.

D. V. HUBBLE.

PUBLIC HEALTH ADMINISTRATION

Principles of Public Health Administration. By John J. Hanlon, M.S., M.D., M.P.H. (Pp. 506; 48 illustrations. £2 2s.) London: Henry Kimpton. 1950.

This textbook is on the administrative basis of the practice of public health in the United States. The first part covers the scope and history of public health and contains an invaluable chapter on the socio-economic justification of public health activities. How often is the medical officer of health faced with the debit column of public health finance—how often has he wished that his vital statistics were convertible currency to be recorded on the credit side? Here is the answer, one which could well be supplied to members of local authority finance committees and their officers for their pleasure and profit.

The second part of the book is on the structure of organization and the detail of day-to-day administration. The reader will find much to interest him in contrasting British methods with American. But although the differences are inevitable it is quite clear that all public health workers are unanimous about the disastrous effects of attempts at false economy in preventive medicine.

The third part presents attractively factual and statistical information about public health activities in the United States. This gives a clear impression of a high level of efficiency. It gives an equally clear impression of much lack of uniformity in administration as between the several States. But this is not necessarily to be deplored; it may well be that avoidance of uniformity is the best way to ensure continuity of progress.

This is a sound, well-balanced, and logical textbook which will be prized also by the discerning reader as a useful work of reference.

C. METCALFE BROWN.

RADIOLOGY OF THE PANCREAS

Roentgen Manifestations of Pancreatic Disease. By Maxwell Herbert Poppel, M.D., F.A.C.R. (Pp. 366; 166 illustrations. £3 17s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1951.

In the preface Professor Poppel says that his main guiding thought has been the presentation of a radiological survey of the anatomy, physiology, and pathology of the pancreas. He first describes the development and anatomy of the pancreas and the possible variations. The anatomy of the duodenum follows. Since it is not possible yet to produce direct radiographic evidence of the shape or functional capacity of the pancreas, pathological changes can be recognized only by indirect methods of examination, unless calcification is present. The many indirect methods are described in detail, including in particular the technique for obtaining an impression of the shape of the pancreatic bed by suitable projections during a barium-meal examination.

The author then gives a systematic presentation of the radiological findings in primary pancreatic disease. Here pancreatic cancer receives adequate attention. The chapter on acute pancreatitis deserves special mention; another is devoted to pancreatic deficiency and its effect on motor function. Comprehensive chapters on secondary lesions of the pancreas and differential diagnoses in suspected pancreatic disease complete the book. Statistical data mainly relating to the death rate in the U.S.A. from pancreatic cancer, a list of nearly three hundred references, and a good index are included.

The author has succeeded in his task and has given his reader a clear account of a difficult radiological subject. His illustrations are of uniformly high quality and they are conveniently related to the text. This book will clearly be a standard work for many years to come.

F. PYGOTT.

FRENCH PSYCHIATRY

Méthodes Biologiques en Clinique Psychiatrique. By Professor Jean Delay. (Pp. 536; 68 figures. 2,000 francs.) Paris: Masson. 1950.

The author of this massive book is professor of psychiatry in the University of Paris, and his work is therefore likely to have a far-reaching effect on the teaching of psychiatry and the direction of research and clinical interests in France. French psychiatry has for the past two or three generations remained rather isolated from the influences which have been dominant in other parts of Europe, in Britain, and in the U.S.A., and since the time of Janet it has tended towards stagnation. Kraepelin, Bleuler, Freud, and Jung have all failed to attract French clinicians away from their preoccupation with the refined subclassification of clinical states along purely symptomatological lines. But recent additions to knowledge provided by physical methods of investigation and treatment have clearly made a strong appeal. Professor Delay has played a leading role in this innovating tendency, and in his earlier books has provided a stimulating contribution.

He attempts to make this book systematic. It consists of three sections concerned with encephalographic methods (electro- and pneumo-encephalography), electro-shock and psychosurgery, and "psycho-chemistry." The last section covers such heterogeneous subjects as psychoses associated with humoral and hormonal changes, the use of penicillin, the treatment of epilepsy, and narco-analysis. The attempt at comprehensiveness is partially defeated by the omission of any discussion of insulin-coma therapy; and it seems to the reviewer that little purpose is served by thrusting into one bag subjects which have essentially little relation to one another. Furthermore, the clinical observations on which the author founds his discussion are for the most part of an individual and anecdotal kind; no large series of patients of any one kind has been systematically investigated. These deficiencies lend the whole work a rather literary quality. Nevertheless the British reader must await with interest the further development to which this new spirit in French psychiatry will lead.

ELIOT SLATER.

INFANT FEEDING

Feeding Mothers and Babies. By Nell Heaton and Guy Daynes, M.R.C.S., L.R.C.P., D.C.H. (Pp. 214. 7s. 6d.) London: Faber and Faber. 1950.

Miss Nell Heaton and Dr. Guy Daynes have managed to give a new approach to a subject upon which there are probably too many books already. They give far more detail and many more recipes than is usual, and the practical tone of the book makes it especially valuable. There are, however, certain errors which detract from its use; their correction is necessary and to some extent urgent. For example, it is a mistake to lump together (p. 77) so-called humanized dried milks and certain half-cream dried milks, for half-cream national dried milk does not contain added sugar. This same muddle is repeated in a table on p. 88. Again (p. 97) the question of the addition of vitamin D to national dried milk is not made clear, nor would the ordinary mother realize from the book that margarine also contains additional vitamin D, probably more than butter in many instances.

In a book where so much detail on diet and cooking is rightly included the mother is left in doubt about whether or not she takes her two slices of bread (at breakfast, p. 23) with or without butter or margarine. Also something has gone seriously wrong with a paragraph on p. 32 giving arguments for and against breast-feeding. Dr. Daynes is no doubt responsible for a bias in favour of glucose water where plain water will often better serve, and he is certainly entitled to his opinion, although it is rather "plugged" by the use of capitals. It is hoped that a new edition will be improved and corrected, for obviously there is much useful information available here.

ALAN MONCRIEFF.

GUIDE TO NURSING

A Guide to Professional Nursing. Nursing, Midwifery, and the Allied Professions. By Bethina A. Bennett, O.B.E., S.R.N., M.C.S.P. (Pp. 231; illustrated. 18s.) London: Faber and Faber. 1951.

The Victorian idea that an educated young woman should not follow a profession or seek a public career is now almost inconceivable. When a girl reaches the age of 16 or 17 she naturally faces the difficult decision which occupation will best suit her disposition and attainments. Many women prefer to have an occupation which in some way, either directly or indirectly, helps to succour the sick, and it is fortunate that all who so wish have ample opportunity of following their inclination. Yet they may be in some doubt about which particular profession they should adopt, and it is for such persons, and for those who may have to tender them advice, that this book is primarily meant.

It is a book of reference giving much useful information concisely. The matter is well arranged and the index makes reference easy. The author discusses not only the professions of nursing and midwifery, but all the other allied professions, so that those who wish to become almoners, speech therapists, radiographers, physiotherapists, occupational therapists, dietitians, chiropodists, orthoptists, or laboratory technicians will all find information relevant to their choice. The author states that it is her intention to keep the facts up to date by issuing yearly editions; this is a wise decision, since there are likely to be changes as the new Health Service continues to develop.

V. ZACHARY COPE.

BRITISH MEDICAL JOURNAL
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SURGERY OF THE OESOPHAGUS

The oesophagus, considered as a tube leading from the pharynx to the stomach, might appear to be a viscus hardly worthy of more than passing regard by anatomists and physiologists. That it can be replaced by an inert rubber tube does not enhance its importance. But observation of the pathological changes in it have raised it to a position of dramatic clinical interest, and the literature on its diseases is rapidly increasing.

Carcinoma of the oesophagus has long been a field for those in search of adventure, and, as so often happens in surgery, the knowledge acquired has led to a keener interest in the non-malignant lesions and a deeper sense of the importance of the physiology of the organ. Direct surgical attack on malignant disease of the oesophagus was long delayed by the technical difficulties of respiratory function with an open pneumothorax and later by the problems of reconstruction. Many patients have suffered, first with rubber gullets and later with antethoracic skin reconstructions of the oesophagus, only to die in great discomfort from secondary deposits. Few have survived. A great advance was made in the treatment of carcinoma of the oesophagus when it was found that the stomach could be mobilized, drawn up into the chest, and anastomosed to the divided oesophagus at almost any level in the mediastinum, for this gave the surgeon a chance to extirpate the growth and restore continuity in one operation. Even if the patient was not to survive very long the price was not so great compared with the multiple stages, the sepsis, and the fistulae of earlier times: palliation at least was achieved.

A glance at a cross-section of the chest at any level down to the sixth dorsal vertebra shows such a packing together of irremovable structures around the oesophagus that even a small margin of normal tissue beyond a growth cannot be obtained. Knowledge of cancer elsewhere suggests that its treatment by surgery when it occurs in the upper half of the oesophagus cannot be anything more than palliative. To add two or three years to a life of 60, however, is no mean achievement if the years of survival can be lived in comfort. As Mr. R. W. Raven shows in this issue (p. 951), it is possible by skilful surgery greatly to relieve the symptoms of such a distressing condition as cancer of the hypopharynx. In the lower oesophagus conditions are more favourable, for there is more cellular tissue and a more radical operation is possible. After early successes in removing the oesophagus had led to the disappointments of metastases, surgeons concentrated their attention more and more on a clean removal of cellular tissue and lymphatic vessels and glands by carefully planned block dissection. In this issue Mr. R. H. Franklin and Mr. J. J. Shipman review the results obtained in 159 patients treated at the Hammersmith Hospital between 1946 and 1949. Their figures show that the disease occurs mostly towards the end of life among people who are in poor physical condition from other causes, and their description of symptoms emphasizes that the disease is usually present for a long time before complaint is made. The ascribing by patients of their first discomfort to indigestion is sometimes easily accepted by their doctors. The authors rightly insist that a negative radiological investigation must not be taken as final, for in seven of their patients the diagnosis was made only by oesophagoscopy. Only one of their patients out of 159 lived for four years, two for two years, and two for eighteen months. These results in terms of years of survival are as discouraging as those of most other surgeons, but it would be quite unfair to make this the sole basis of assessment, for only the patients themselves and their relatives can say what relief and comfort they have had. An operative mortality (survival for less than a month) of 51% is high, but this may reflect the advanced state of disease with which these surgeons have been confronted.

The stimulus of surgery has done much to revive the interest of the physicians in the work of the endoscopists, for non-malignant lesions of the oesophagus have been well described for a long time by those who used the oesophagoscope. In a paper by Dr. J. B. Harman in this issue proper acknowledgment is made to Chevalier Jackson and his school for their great contribution to the study of oesophagitis, but it should be mentioned that Negus in this country devised and used the oesophagoscope that really made the inside of the oesophagus visible to the less trained eyes of physicians and surgeons. Now that oesophagitis is becoming almost a popular diagnosis Harman's description of the condition is most timely. As he says, "These symptoms are as stereotyped as those of peptic ulcer," but he rightly warns against the confusion that may arise when patients with cholecystitis

1 *Surg. Gynec. Obstet.*, 1951, **92**, 419.

or duodenal ulcer complain of the same symptoms. There are those who would disagree with the statement that the pain "does not show periodicity over weeks or months like a peptic ulcer," and it is interesting that during a long remission of symptoms an oesophagoscopic examination will show the mucosa to be just as inflamed and ulcerated as at other times. Although it is true that we still do not know "how common oesophagitis is, how often it exists without symptoms, or how often symptoms mean oesophagitis," patients suffering from oesophagitis are being so thoroughly investigated in many centres to-day that statistics will soon be available. In the meantime Allison[1] has given some idea of the position. He found that, of 176 patients with sliding herniae, 63 had chronic oesophageal ulcers with stenosis, 73 had macroscopic superficial oesophagitis with ulceration, 21 had no visible oesophagitis, and in 19 the findings were indefinite. The treatment of reflux oesophagitis is surgical and, as Harman emphasizes, "should be based entirely on the severity of the symptoms," though he would no doubt agree that this should include also a consideration of the certainty with which surgeons can promise success. If the record of such easily assessable treatment as that of inguinal and femoral hernia is any guide to what may be expected in the surgery of diaphragmatic hernia, treatment of oesophagitis will be in a confused state for some time. Perhaps it is a forewarning of the arguments to come that Harman, in suggesting resection for peptic stricture of the oesophagus, says, "The stomach must not be drawn up into the thorax, for this again leaves the patient with the stage set for return of the trouble"; but he adds that a tube made from the greater curvature of the stomach may be tried. It may be some time before a satisfactory equilibrium is established between the surgeons who bring the stomach, or part of it, up into the mediastinum and those who push it down into the abdomen. The conflict has been by-passed by those who use jejunum for reconstruction.

EPIDEMIOLOGY OF HYPERTENSION

Hypertension remains among the least understood of the major afflictions of Western man. In an admirable review published in our opening pages this week Professor J. McMichael surveys the methods of treating this common condition. No one knows how many people are hypertensive, but with over 40% of our population above 40 years of age there must be hundreds of thousands, if not millions, of men and women with pressure readings temporarily or permanently higher than is now considered "normal." Very large numbers, too, must suffer and die of the cardiac, cerebral, or renal complications of hypertension—although, because death certificates are clinically incomplete records, we do not know the prevalence even of these gravest manifestations of the disease. The origins of high pressure are virtually unknown—"essential"—despite a most intensive series of laboratory researches in recent years. A forthcoming bibliography on blood pressure from Columbia University promises to list "18,000 articles in 20 languages." Yet, the dangers of obesity apart, there is nothing on which to base a realistic policy of prevention. In the circumstances it is not surprising that there is growing interest in the possibility of an epidemiological approach to the problems of hypertension, as of other chronic diseases whose causes are unknown, a subject we referred to recently[1] in connexion with coronary heart disease in medical practitioners.

The epidemiologist studies a group, and the questions that he often puts may be phrased—who, in which circumstances, develops what? On hypertension he might expect answers to *who*, in terms of such variables known (or suspected) to be relevant as sex, age, heredity, physique, habits, personality structure, and modes of physiological response to stress. Under *circumstances* might be considered physical, nutritional, occupational, economic, and psychological environments. *What* sort of hypertension might mean only high pressure readings, or symptoms, complications, or death from hypertension and its associated disorders. In the United States of America long-term epidemiological and analogous inquiries are already in operation. Under the auspices of the U.S. Public Health Service, and with the co-operation of the State Health Commission and of the local profession,[2] about two-thirds of all the men and women aged 30–59 years in the town of Framingham, Massachusetts, roughly 6,000 altogether, are being given an exhaustive historical and physical, though rather disappointingly slight psychological and social, examination as a base-line for what is intended to be a 20-year follow-up study. The investigators hope to clarify the beginnings of hypertensive, coronary, and other cardiovascular diseases of middle age in a "normal" population of sufficient size. A special staff has been organized, "including the examining physicians; a clinic nurse; *x*-ray, electrocardiography, and laboratory technicians;

[1] *British Medical Journal*, 1952, **1**, 535.
[2] Dawber, T. R., Meadors, G. F., and Moore, F. E., *Amer. J. publ. Hlth*, 1951, **41**, 279.
[3] Thomas, C. B., *Bull. Johns Hopk. Hosp.*, 1951, **89**, 419.
[4] *Circulation*, 1952, **5**, 215.
[5] *A Symposium on Essential Hypertension—An Epidemiologic Approach*, 1951, Boston.
[6] *British Medical Journal*, 1952, **1**, 503; *Lancet*, 1951, **1**, 1, 69.
[7] *British Medical Journal*, 1952, **1**, 808.

statisticians; interviewing and administrative clerks; a health educator; and visiting consultants in the field of cardiology, electrocardiography, roentgenology, pathology, and biochemistry." It is estimated from a sample study that roughly 5,000 subjects will be free from recognizable cardiovascular disorder at the time of the initial examination, and that about 400 of the 5,000 may develop something within five years. Interesting results should therefore begin to be available soon.

At Johns Hopkins the department of preventive medicine[3] is making use of the well-known fondness of doctors for their alma mater to start what is intended to be an even longer cardiovascular follow-up. Medical students are being subjected to a very elaborate inquiry with "detailed hereditary studies; studies of the cardiovascular system at rest and under stress (cold pressor test, exercise test, controlled anoxaemia test); studies of metabolic patterns (diet, nutrition, blood cholesterol, circulating eosinophils, acute sodium withdrawal) and studies of personality (habit survey, family data, Rorschach test)," and they will be followed for years after qualification.

This type of investigation owes much to epidemiological work previously done on other diseases, and it combines advantages of the laboratory, the bedside, and the population study. It has already been found that the circulations of far more of the students with some parental history of hypertension and coronary disease are particularly reactive to exercise than is the case in those with a negative family history. Further, those with such a parental history have different patterns of *nervous* response to stress from the others. Ancel Keys and his group in the Laboratory of Physiological Hygiene at Minneapolis are also conducting a functional and pathological cardiovascular investigation of a special "normal" population—some 300 white-collar, middle-class men—and some have now been followed for four years. First results are beginning to be published.[4]

A conference at Boston was called last year by the Commonwealth of Massachusetts, and the School of Public Health and the Bureau of Applied Social Research of Columbia University, to launch a still further epidemiological survey on the problems of hypertension. The report[5] of the meeting opens with an account of the present state of our knowledge in an illuminating series of papers by some of the leading American authorities. It is hoped that medical and social scientists can jointly carry out a long-term community study, to provide facts on such matters as the definition of "essential" hypertension, the prevalence of hypertension by race and age, the natural history of the disease in man, the significance of the prehypertensive state, and blood-pressure levels in relation to pregnancy, injury, infection, work habits, and major psychological trauma. The approach is perhaps too closely restricted to hypertension; clinical experience would certainly indicate equal attention at the same time to its partner in pathology, atheroma.

In Britain the National Health Service should offer opportunities for the conduct of such studies of the natural history of disease in populations. As Morris and his colleagues have pointed out,[6] simple methods and small numbers may be sufficient to give worth-while results. If a number of factors are involved in the beginnings of hypertension the epidemiological approach might be particularly useful. The Department of Health for Scotland, which is showing such a lively interest in the problems of coronary disease,[7] may well be able to set an example by initiating field studies of hypertension also; and the hopes of Sir James Mackenzie, who founded the Institute for Clinical Research at St. Andrews, may yet be fulfilled.

THE GROWTH AND DEVELOPMENT OF CHILDREN

The methods of studying growth and development are at present in the melting-pot and there is great need of some new moulds into which to pour the fresh material. The volume of a child's body, its surface area, the changes in biochemical substances, and the function of the endocrine glands may all have to be taken into consideration. Tanner,[1] in a stimulating discussion of the assessment of children's growth and development, emphasizes the complexity of the subject and puts forward constructive ideas about the future handling of data. Physiologists, psychologists, and biochemists are all interested in growth and in seeing that information about it is collected in the right way. But it is those in charge of the health of children who particularly want to know: Is this child growing normally? The attempt at the answer to this question forms the major part of Tanner's paper. Standards of so-called normal children's measurements are needed for the assessment of children's growth. These can be obtained in two ways: either by measuring large numbers of children at various ages, or by regularly taking the measurements of the same children over, ideally, the period of birth to maturity. The first method provides information about how far "normal" children have developed by a certain age—in other words, it is a "distance study." The second method—a "velocity study"—shows how much a child has grown in, say, the last year. The information given by finding out the child's velocity of growth is probably more useful than that given by comparing its measurements at any given age with those of other children at the same age.

Reliable normal standards are, of course, needed to detect abnormalities, but even with these a decision on what is abnormal is still difficult. Tanner discusses this problem statistically, but the most that can be said at present is that, if a child's measurements are found to be at either end of a distribution curve, then we should be suspicious. Distance (or cross-sectional) standards for height and weight are available in this country, mainly from the work of Gore and Palmer[2] and Daley,[3] but there are some failings in both these sets of standards and more are needed. There are no published figures in this country for any measurements other than height and weight, and as yet there are no standards for velocity (or longitudinal) measurements available in the British Isles, and for purposes of comparison American figures have to be used. These velocity studies are costly and difficult, but the results of even small-scale studies would be of great value, provided the data were correctly collected and always in the same way. Unless anthropometric measurements, including height and weight, are made by trained workers with great care, the results may be not only useless but confusing. It is, for instance, surprising how many children lose height during the course of some studies. Particularly difficult is the measurement of younger children and infants.

There are three longitudinal studies in progress in this country : one of these is well established at the National Children's Home, Harpenden, jointly sponsored by the Ministry of Health and the Sherrington School of Physiology at St. Thomas's Hospital. This research embraces many aspects of growth, but it is not possible to follow the children from birth. There is only one study planned from birth to maturity, and that has just been started at the Child Study Centre, jointly run by the Institutes of Child Health and Education in the University of London. This centre is also investigating and attempting to develop new methods of measurement of children. A third study is being carried out at the Institute of Social Medicine at Oxford. There would seem to be a real need for an advisory body—international if possible—to help such studies to start and progress in unison.

In the study of growth a decision has to be made on the measurements which are to be taken. Stuart and Meredith[4] have pointed out that height is only one aspect of size and that weight does not tell us where the weight is—for example, whether in fat or muscle. Therefore they urged that in order to obtain a true picture of the growth of a particular child five other measurements be taken to determine linearity, muscular development, and subcutaneous tissue. Obviously the ways of recording growth are legion, and the more measurements that are made the more complex is the chart of a child's growth going to appear. Even the statisticians are not by any means agreed on how growth should be recorded, though Tanner gives some useful suggestions for future experiment.

1 *Arch. Dis. Childh.*, 1952, **27**, 10.
2 *Lancet*, 1949, **1**, 385.
3 *Report on the Heights and Weights of School Pupils in the County of London in 1949*, 1950, London.
4 *Amer. J. publ. Hlth*, 1946, **36**, 1365.

ACETYLCHOLINE TREATMENT IN PSYCHIATRY

The undeniable success of electric convulsive therapy mainly in depressive states has encouraged research into other physical treatments in psychiatry. Acetylcholine "shock" is the latest to be discussed at a meeting of the Section of Psychiatry at the Royal Society of Medicine. Professor López-Ibor, of Madrid, and Dr. W. Sargant outlined their experiences up to date with a method importantly different from that which Fiamberti[1] used in his original technique. Fiamberti's aim was to produce a major convulsion by the rapid intravenous injection of up to 0.6 g. of acetylcholine. The physiological mechanism provoking the seizure is still under some dispute. Such an injection brings about cardiac standstill, and it has been thought that the resulting anoxia causes the convulsion.[2] It is possible, however, that some of the injected acetylcholine does reach the central nervous system in spite of its very rapid breakdown in the body. Acetylcholine applied directly to the cortex can produce convulsions,[3] and therefore both direct and indirect effects may contribute to the onset of the fit. Professor López-Ibor's method, however, is to inject a smaller quantity of acetylcholine, insufficient to cause a convulsion. There is a short period of intense parasympathetic stimulation, but of course no long-lasting direct effects, since acetylcholine is so rapidly destroyed. A short period of unconsciousness appears to improve the therapeutic effect. In Madrid the patients who seemed to respond best were suffering from what may be called mild cyclic anxiety depressions. Sargant, with a less extensive experience of this form of treatment than Professor López-Ibor, was inclined to favour it for longer-standing neuroses in which tension was marked.

The efficacy of such treatment is surprising in view of the well-confirmed lack of success of electric-shock treatments which fail to cause a major seizure, and it is not clear why acetylcholine should be effective in subconvulsive doses. Acetylcholine is, of course, almost ubiquitous in the central nervous system, in which it has a very rapid metabolic turnover. It is not likely, therefore, that any continued direct action of the injected drug on the central nervous system is important, even if it exists. The parasympathetic effects are likewise evanescent, though intense, and tolerance seems to be fairly rapidly acquired by repeated injections. If such tolerance affects endogenously produced acetylcholine and alters the sympathetic-parasympathetic balance, then this may provide an explanation of its therapeutic effect. Another possibility is that the disturbing physiological events resulting from the injection of acetylcholine constitute yet another stress calling into action the "alarm reaction," a concept perhaps more fashionable than explanatory. Whether there is some more specific effect remains to be seen, and the preliminary studies at St. Thomas's Hospital which Dr. Sargant described are an interesting start to elucidating this drug's mode of action. The

1 *Riv. oto-neuro-oftal.*, 1940, **17**, 265.
2 Ajmone-Marsan, C., and Fuortes, M. G. F., *Electroenceph. clin. Neurophysiol.*, 1949, **1**, 283.
3 Forster, F. M., *Arch. Neurol. Psychiat., Chicago*, 1945, **54**, 391.

present lack of knowledge should not hinder further clinical study, since the results so far reported are encouraging, and psychiatrists are properly not chary of using treatments only empirically based.

ARTERIOTOMY

The preoccupation of modern anaesthetists with lowering their patients' blood pressure springs from the work of W. J. Gardner,[1] of Cleveland, who introduced arterial bleeding and retransfusion to lessen haemorrhage in neurosurgery. Since his paper in 1946 anaesthetists have favoured the more convenient methonium compounds, but arteriotomy has continued in use for craniotomy and fenestration. The technique has been successfully used by Hale[2] in 50 cases, by Mortimer[3] in 19, and by Bilsland[4] in 63, though in three instances Bilsland suspected that the method contributed to his patient's death.

Blood may be drawn from an incision in the radial artery into a standard bottle containing sodium citrate, to be replaced later by means of air pressure through tubing irrigated with heparin; or it may be taken into the closed apparatus designed by Mortimer. Blood is withdrawn in amounts of 500 ml. or less at a time, until the systolic pressure reaches 80 mm. Hg; the total may vary from 300 ml. to almost 3 litres. The blood can be returned—at the end of the operation, or before if necessary—more rapidly than intravenously and with more effect: Bilsland claims a sustained rise from a systolic pressure of 60 mm. Hg to normal when 100 ml. of blood was replaced in one minute. This rise is apparently due to an immediate improvement in the coronary circulation, the outstanding benefit claimed for intra-arterial transfusion.

A lowered blood pressure and arterial constriction are indisputably useful conditions in a branch of surgery where bleeding often hampers and may limit the operation. To obtain them by controlled exsanguination nevertheless introduces the hazard of a dangerous intolerance of anoxia, the possibility of the circulatory depression becoming irreversible, and the consequences of ligation or thrombus of the radial artery (though the disturbance to the circulation in the hand is usually transitory). There is also the danger of haemodilution in response to a large amount of blood leaving the body. Hale recognized this risk by withholding 500 ml. of blood from some of his patients. Borri and Matellis[5] gave the warning that forcibly returning all the patient's blood against the resistance of vasoconstriction might cause dilatation of the heart. They accept the theory that haemorrhage liberates an enzyme causing compensatory vasoconstriction, and they obtained bloodless operation fields in dogs by removing only small amounts of blood. Borri and Matellis believed that the removal of as little as 500 ml. of blood from a patient could produce a dry operating site, and this seems in accordance with the successful results of arteriotomy that have sometimes followed the withdrawal of small quantities of blood.

1 *J. Amer. med. Ass.*, 1946, **132**, 572.
2 *Anesthesiology*, 1948, **9**, 498.
3 *Anaesthesia*, 1951, **6**, 128.
4 Ibid., 1951, **6**, 20.
5 *Lancet* 1951, **2**, 489.

PNEUMOCONIOSIS IN GOLD MINES

The subject of pneumoconiosis in the Kolar gold field, South India, was discussed at a recent meeting of the Institution of Mining and Metallurgy, and some comparisons were made with the disease in the Witwatersrand in South Africa. Mr. H. H. Watson, who has been investigating the conditions in the Kolar gold field, said that a pneumoconiosis similar in many ways to that found among coal workers in Great Britain was common among those who had worked for long periods underground in Kolar. It was not very disabling unless complicated by tuberculosis. The only important similarity with silicosis as seen, for instance, in the Witwatersrand gold mines was an enhanced susceptibility to tuberculosis. In the three years 1946–8 the number of underground employees was 13,800, 14,500, and 14,300 respectively,, and the number compensated for pneumoconiosis (all stages) was respectively for the three years 180, 174, and 113. Very high dust concentrations are common in the Kolar mines, and it is surprising that the severity and prevalence of the disease are not greater. Dust suppression provides some very difficult technical problems, for the very high underground temperatures—120° F. (48.8° C.) dry-bulb, and 90° F. (32.2° C.) wet-bulb in development ends—preclude the use of water, except on a very small scale.

The dusts of Kolar are apparently much less dangerous than the rock dusts of the Witwatersrand, and the explanation is thought to lie partly in differences in the quartz content. Experiments on animals have shown that Kolar quartz is potentially as dangerous as any other quartz dust, and Mr. Watson suggested that the difference in quartz content in the two fields may not be a sufficient explanation, and that the Kolar dust may be rich in a mineral which modifies the action of the quartz in the lung. An untested theory is that a small amount of free silica may be rendered less harmful by excess of lime. The percentage of calcium (as CaO) in the airborne dusts in the Kolar gold field is 10–12, and in those of the Witwatersrand 0.6–4.2. Unfortunately information on the quartz content of the respirable fraction of both Kolar and Witwatersrand dusts is lacking.

At the same meeting a mining engineer from South Africa, Mr. C. O. Reid, gave the latest figures of the Silicosis Medical Bureau of Johannesburg for new cases of silicosis. Out of some 28,000 miners examined each year the number of new cases of silicosis in three recent years was respectively 207, 388, and 220. The number of new cases of tuberculosis in the same three years was 23, 32, and 12, but in two of the years only one new case of tuberculosis with silicosis was found, and in the third year no case at all. All the cases of silicosis were in the first stage.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

HEART BLOCK

BY

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Heart block can be defined as a condition in which the impulse from auricles to ventricles is partially or completely interrupted. This interruption may involve the main stem in the bundle of His, in which case, although the impulse is from time to time slowed or permanently arrested, the method of spread in the ventricular muscle beyond this obstruction is normal in type. Bundle-branch block is a condition in which partial or complete interference occurs in the transmission of the impulse down either the right or the left branch of the bundle. Bundle-branch block may occur in cases of ordinary heart block.

Lesions of the Main Bundle

The bundle of His may be affected by some pathological process in such a manner that the transmission of the impulse from auricles to ventricles is slowed down but not obstructed. This condition is known as latent heart block, for no ventricular beats are dropped out, and there is no clinical evidence of the presence of the block. In the next stage beats are dropped from time to time when the transmitting power of the bundle begins to tire. After a dropped beat, however, the bundle is rested so that the transmitting time picks up again. This is called the stage of dropped beats (Fig. 1). These two varieties of heart block are slight in degree; they are usually found in acute conditions such as diphtheria or acute rheumatism. The pause of a dropped beat is silent: in the pause due to a premature beat the extrasystole can always be heard through the stethoscope, if it is carefully listened for. In low-grade heart block the loss of function of the bundle is an indication of the general effect of the toxin or the disease upon the state of the heart muscle as a whole.

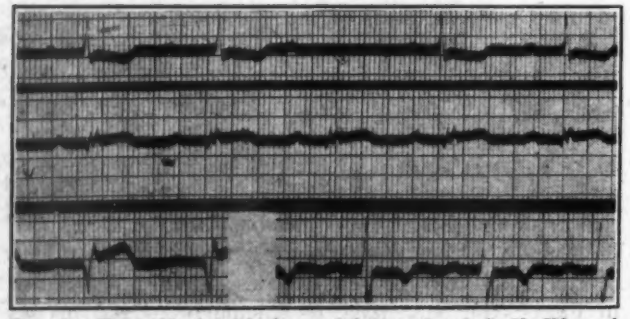


FIG. 1.—*Heart block with dropped beats.* Leads I, II, III, and CR4. In Lead I the P–R interval of the first two beats is 0.28 and 0.36 second respectively. The third auricular impulse fails to traverse the bundle of His, and no ventricular response is evoked. The ST changes of a recent posterior infarct are also present.

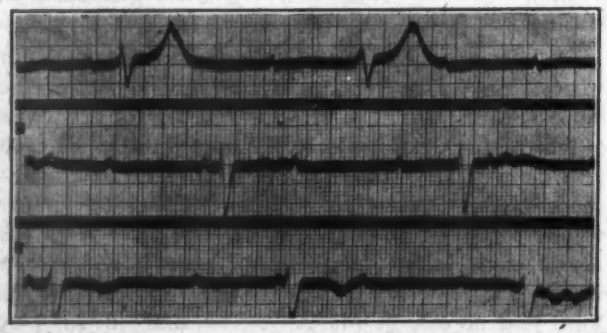


FIG. 2.—*Complete heart block.* Leads I, II, and III. In Lead II it is clear that the regular P waves have a rhythm which is quite independent of the QRS or ventricular complexes.

More severe grades of heart block are as a rule found in more chronic pathological states, the lesion affecting the bundle being often a local one, generally arteriosclerotic but occasionally syphilitic. The usual arterial supply to the bundle of His is a separate branch of the right coronary artery, so that heart block is an infrequent complication of coronary thrombosis, which generally involves this vessel lower down. Congenital varieties of heart block are not uncommon, constituting perhaps 10% of all cases of high-grade block. Heart block usually occurs in auricular flutter, where the auricular rate is usually 200 beats a minute or more. This high auricular rate over-stimulates the bundle of His and fatigues it. The heart block in this condition does not indicate disease of the conducting tissues.

The more severe grades of heart block usually involve a delay in the bundle sufficient to stop many of the impulses from auricle to ventricle. The usual varieties found are 2:1, 3:1, or complete block. In 2:1 block every other auricular impulse fails to reach the ventricle. In 3:1 block two out of three fail to do so, and in complete block no auricular impulses are transmitted to the ventricle. In the latter condition ventricular activity is evoked by a separate pacemaker situated in the bundle of His above its division into two branches. From this position, usually at a regular rate of from 30 to 40 beats a minute, impulses arise and stimulate the ventricles to contract (Fig. 2).

Effect of Heart Block on Cardiac Function

Partial heart block in which few of the beats fail to reach the ventricle from the auricle has no significant effect upon the cardiac function. The heart muscle, however, is considerably weakened by the general myocarditis of which this slight degree of block is a sign. Clinically, therefore, the presence of this slight block is valuable as an indication of myocardial weakness. These types of block are as a rule recovered from completely if the patient survives the acute disease. This recovery in the case of acute rheumatic carditis may be unexpectedly good. I have seen three patients, all of them adolescents or adults, who suffered from acute rheumatic carditis so severe as to cause pericarditis, high fever, and an unusually high grade of heart block. In spite of the severity of the disease and its widespread effect on the heart, all of these patients made a perfect recovery and were able to return to normal physical activities in course of time. They remained well for a number of years before they were lost sight of.

High-grade heart block presents a different type of physiological problem. The best example is complete block in which the ventricles are beating at a speed of 30 to 40 beats a minute. The bradycardia of necessity causes a long diastole. This has a number of important results: the ventricles are well filled; a big stroke output follows; the ventricles are stretched and a little enlarged; the systolic pressure is raised; the diastolic pressure is lowered; the coronary flow is prolonged. There are three clinical points, therefore, which must be remembered in heart block with bradycardia in order that the patient's true physical condition shall not be misunderstood. Some enlargement of the

ventricles is physiological in heart block, therefore part of the cardiac enlargement can be disregarded. The raised systolic blood pressure in such cases does not mean hypertension; a systolic reading of 180 to 190 is physiological. Finally, when this systolic pressure is associated with a diastolic reading of 70 to 80 this very big pulse pressure is also a physiological result of the bradycardia, and is not due to aortic regurgitation or to any similar pathological process.

A further result of heart block, which is not physiological in origin but due to a direct extension of the causative disease to the neighbourhood of the idioventricular pacemaker in the bundle of His, is seen in the form of Stokes–Adams attacks. When disease affects the activity of the ventricular pacemaker its function becomes unreliable and in some cases it ceases work completely, bringing the ventricles to a standstill. When the standstill lasts for four seconds or more the result is transient giddiness. If the period is prolonged further a brief spell of unconsciousness occurs. Should the time be longer still the unconscious patient suffers from generalized convulsions. During the Stokes–Adams attack there is no pulse at the wrist and no evidence of cardiac activity on listening with the stethoscope. Pallor followed by cyanosis occurs during the period of ventricular standstill, and also deep breathing. At the end of the attack, as the patient comes round, the body flushes red and very often breathing stops for a space, since the previous hyperpnoea has washed out most of the carbon dioxide from the blood stream. The chief diagnostic points suggesting a Stokes–Adams attack are: complete cardiac standstill; an abrupt onset; a duration averaging five to twenty seconds and not exceeding thirty seconds; and rapid and complete recovery to a normal state. Epilepsy, true or arteriosclerotic, vasovagal attacks, and the rare syncopal attacks of auricular flutter and aortic stenosis must be excluded.

Prognosis

The outlook in these high grades of heart block due to chronic myocardial disease is generally not too good, the average expectation of life being about five years. In trying to assess the prognosis, due attention must be paid to other factors such as a history of coronary disease, much enlargement of the heart, nocturnal paroxysmal dyspnoea, and so on.

Treatment

The treatment of the minor degrees of block which are seen in acute infections is that of the acute infection. Complete block and high-grade block need no treatment as such, but if heart failure is present the patient should be treated by rest in bed, mercurial diuretics, intravenous or intramuscular aminophylline, and by digitalis. The bradycardia of heart block is no contraindication to the use of digitalis if congestive failure is present. Digitalis acts by depressing the conductivity of the bundle of His. If this conductivity is already so depressed as to have become complete it is quite clear that the action of the digitalis has been forestalled, and that the drug cannot have any more effect upon the already slowed heart rate. In other words, digitalis cannot make more complete what is already complete.

Stokes–Adams attacks are usually so brief that treatment cannot be administered during them. Therapy must therefore be concentrated upon prevention. In most cases ephedrine hydrochloride, 1 gr. (65 mg.) by mouth three times a day after meals, is efficacious in preventing the attacks. In some cases the dosage may be less than this and in others it needs to be more. If ephedrine does not act perfectly its effect can sometimes be enhanced by atropine. This also can be given by mouth at the same time as the ephedrine, and the dosage again will vary from case to case: sometimes 1/200 gr. (0.32 mg.) three times a day will suffice, but in others the adequate dose will be found to be 1/100 gr. (0.65 mg.) or even 1/75 gr. (0.87 mg.). Should ephedrine be found inadequate adrenaline may be given two or three times daily by injection subcutaneously or intramuscularly. The dose should be 0.5 to 1 ml. Sublingual isoprenaline may also be tried. Quinidine inhibits the activity of the idioventricular pacemaker, and its use in high-grade heart block is therefore very dangerous.

Bundle-branch Block

The myocardial lesion which involves one or other of the branches of His, and which leaves the main bundle unaffected, may occur in either acute or chronic conditions. Diphtheria, myocarditis, and acute rheumatism are again the most outstanding acute infective causes. The abnormality is only part of the general myocardial disease and its clinical importance is subsidiary.

Chronic bundle-branch defects may roughly be placed in one or other of two categories. In the first group the lesion may be one of several or of many other evidences of organic cardiovascular trouble. It may coincide with chronic coronary disease, aortic valve disease, or hypertension, and may be associated with symptoms of myocardial failure. Here it is merely one of many proofs of organic heart disease, and it is insufficient as such to add to the seriousness of the general situation. It can also be a manifestation of a cardiac infarct, appearing during the acute stage and disappearing as the patient recovers.

The second category is that in which a bundle-branch lesion, right or left, seems to be an isolated phenomenon, or at any rate the most outstanding abnormality present. In such patients the heart may not be enlarged or its enlargement may be slight and the function of the heart muscle may be good. One such patient when first examined 16 years ago had a normal electrocardiogram. At his next examination two years later a bundle-branch lesion was discovered. He has since remained in good health in spite of his cardiographic abnormality and is now aged 63. The electrocardiogram of a right or a left bundle-branch lesion is a sufficiently obvious deviation from the normal to constitute a picture in black and white which of itself might be frightening enough to give rise to unduly careful treatment or an unnecessarily bad prognosis (see Figs. 3 and 4). It is therefore important to realize that when a bundle-branch defect is the only major abnormality present, undue attention should not be focused upon it. The important points in

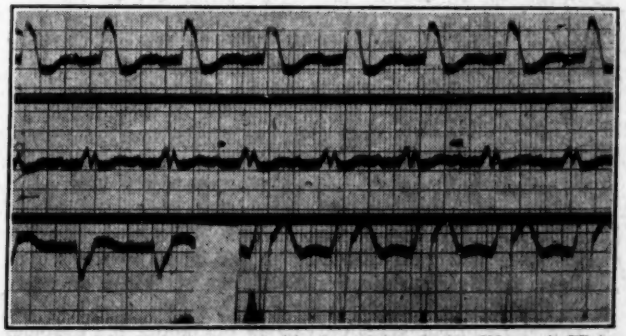


FIG. 3.—*Left bundle-branch block.* Leads I, II, III, and CR4. Note the slurring and the great prolongation of the QRS complexes in all leads. This is the constant characteristic of bundle-branch block.

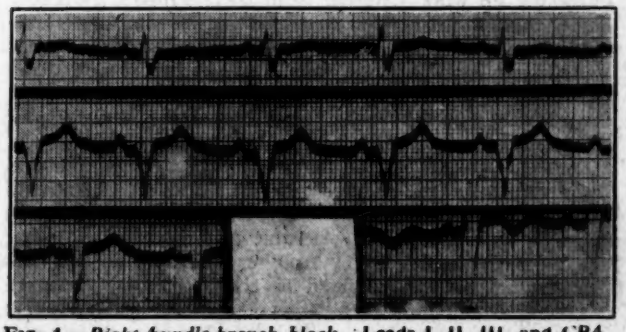


FIG. 4.—*Right bundle-branch block.* Leads I, II, III, and CR4. The QRS is prolonged to 0.16 second. The S wave is deep and slurred in Lead I.

such cases are the heart size and the capacity of the patient to undergo exercise. If the heart is normal in size and if the patient suffers no shortness of breath or other significant symptoms, the bundle-branch lesion may be almost disregarded.

A bundle-branch lesion in other patients may occasionally be part of a latent but more extensive damage to the bundle of His. Such cases may be examined fairly often and yet be found to have a heart rate which is normal and without dropped beats; but in spite of this they are subject to sudden short fainting attacks. These are due to the fact that the idioventricular pacemaker is involved in the pathological process, so that from time to time a more extensive heart block intervenes with cessation of the idioventricular pacemaker and the onset of Stokes–Adams attacks. The important diagnostic points here are the presence of the bundle-branch lesion and the fact that the Stokes–Adams attacks are typical.

Next Refresher Course Article.—"Treatment of Burns," by Dr. J. P. Bull and Mr. D. M. Jackson.

A CANCER RESEARCH JUBILEE

Fifty years ago—in April, 1902—a public appeal was made for the establishment of a fund to be devoted to the investigation of the cause, nature, and treatment of cancer. Some £30,000 was quickly subscribed, and in July of that year the Royal Colleges of Physicians and Surgeons consented to take control of the investigation by setting up a general committee to formulate a scheme of research. In a supplement to the annual report of the Imperial Cancer Research Fund, presented at the recent 49th annual meeting, the work of the ensuing 50 years is described.

The first chairman of the fund was Sir William Church, who at the time was President of the Royal College of Physicians. He remained in the chair for 22 years. His successor, Dr. Sydney Martin, died in the year of his appointment, and was followed by Sir Humphry Rolleston, who served for 15 years, and he by the present chairman, Professor H. R. Dean. Sir Henry Morris, who was the leading spirit in the original discussions, was the first treasurer, to be succeeded by Sir William Watson Cheyne, Sir George Makins, and the present holder of the office, Sir Holburt Waring. The fund has had four directors. Dr. E. F. Bashford was the first, and it was largely due to his initiative that the first scientific reports attained such importance. He was followed in 1914 by Dr. J. A. Murray, who served until 1935; and he by Dr. W. E. Gye, now pursuing research in the field of cancer in Australia, and Dr. James Craigie, the present director. The earlier laboratories were in rooms allocated to the fund by the Royal Colleges in their examination halls, but in 1936 a property at Mill Hill was secured.

The story of the research carried out under the auspices of the Imperial Cancer Research Fund runs parallel with that in other laboratories. Much useful inquiry has been initiated by the Fund itself, but more perhaps has been done by taking up work reported from other sources, especially Continental and American, and assessing its value and carrying it further. When the Fund started operations cancer statistics were in a chaotic state, and one of the first pieces of work was to discover whether the alarming rate at which cancer was reported to be increasing at the beginning of this century was a true increase or whether it was due, thanks to greater attention to clinical recognition and improved diagnostic methods, to the discovery of hitherto "missed" or "inaccessible" cancers. It was found that most of the increase was referable to "inaccessible" sites, the stomach particularly. Another question tackled was whether cancer was confined to civilized races, and as a result of examination of a large number of specimens sent to the laboratories it was declared that cancer occurred among all races and in all climates throughout the Empire.

Again and again in this short history one is reminded of landmarks in cancer research: the work of Jensen on tumour transplantation, which was followed up in these laboratories; Warburg's discovery of aerobic glycolysis in cancer cells, which stimulated much new work on metabolism, although later some of his generalizations proved untenable; the announcement by Rous that a sarcoma of the domestic fowl could be communicated by means of cell-free preparations obtained by mincing and grinding the tumour; Shope's discovery of a tumour virus in the cotton-tail rabbit; Bittner's work on the transmission of mouse cancer by the mother's milk. Then there has been a vast amount of work done on cancers caused by exposure to irritating substances such as tar, and in the wide field of carcinogenesis in general. All this and much more has engaged the laboratories of the Fund, and notable contributions have been made by the scientific staff.

Perhaps, looking back on this history, a warning given by Dr. J. A. Murray, then director, as long ago as 1931 may still be appropriate. He begged the lay and the general medical public to appreciate the conservative and cautious attitude which those engaged in cancer research preserve towards the recurring extravagant announcements of new methods of treatment of cancer. The idea that it is all a gamble, and that success is equally likely to fall to the ignorant as to the instructed, should be discarded. To quote Murray: "Whatever the future of the cancer problem may be, it is certain that it will not yield to the sound of the trumpet."

Reports of Societies

SPREAD OF INFECTION IN THE FAMILY

At a meeting of the Section of Epidemiology and State Medicine of the Royal Society of Medicine on April 18 there was a discussion on "The Spread of Infection in Families." Introducing the speakers, the president, Professor ROBERT CRUICKSHANK, pointed out the special interest of the family as the smallest epidemiological unit and the opportunities it presented for valuable observations by the general practitioner and the paediatrician. Such observations had been made in the past by Snow and Budd, and recently by Pickles, of Aysgarth.

Dr. W. C. COCKBURN, outlining the essential facts to be obtained in the investigation of infectious disease, said that, so far as the family was concerned, these were few and simple: the date of onset of illness and the age, sex, position in the family for the first case, and the number and type and date of onset of symptoms in the household contacts. For most investigations bacteriological co-operation was necessary; he instanced the American observations on the relative frequency of poliomyelitis virus in the excreta of the household and of less close contacts. Epidemiological information of this sort could be used for the following purposes: (1) The study of the "spreading power" of the disease: something was already known of the similarity of salmonella and shigella infections in this respect. (2) The mode of spread—for example, did this differ when the first case was in a child, an adolescent, or an adult? (3) The effect of age on susceptibility. (4) The relation of numbers of clinical cases to persons harbouring the organism without symptoms: recent analyses of food-poisoning infections in this country, carried out by the Public Health Laboratory Service, had shown that in family outbreaks there was a surprisingly high proportion of symptomless excreters. Dr. Cockburn believed that the difficulty of knowing the precise time of infection in a family made family studies less valuable for determining incubation periods.

Whooping-cough and Measles

Recent work on the evaluation of prophylactic agents had incidentally yielded interesting information about the spread of pertussis within the family. Inquiries connected with

the Medical Research Council trials of whooping-cough vaccines had shown a strikingly high attack rate in susceptible children exposed to contact in the family, the average in 10 trials being 87%. This figure was in close agreement with the figures of 98, 90, 89, and 83% (average 90%) recorded in four American trials. The figure varied little at different phases of the epidemics or at different times of the year. So reliable did this secondary familial attack rate appear to be that it was proposed to make more use of it, in families in which one child was inoculated and another was not, as an economical method of estimating the potency of vaccines in place of more extensive follow-up observations.

As an example of the way in which the practitioner could help, Dr. Cockburn described work done by himself and Dr. J. C. McDonald in assessing the value of gamma globulin in modifying measles in exposed children, aged 6 months to 5 years. The practitioners were asked to classify the effects of a standard dose in modifying the severity of the disease and in inhibiting the macular rash. The unexpected finding was that about the same percentage of children had no attack or a modified attack whether the gamma globulin was given before the fifth day after exposure (81%), between the sixth and eighth days (82%), or on the ninth or subsequent days (83%). More observations of this nature were clearly demanded.

Streptococcal Sore Throat

Dr. R. E. O. WILLIAMS gave an account of the natural history of streptococcal infection in a children's home over a two-months period. The "family" here consisted of groups of 10 to 20 children in cottages presided over by one to three adults and sometimes a number of nurses, the age groups consisting of babies, toddlers, and children over 6 years of age. Most of the older children attended one school. For purposes of the present discussion only happenings within the family were considered.

Of the 223 sore throats in the children and the 68 sore throats in the staff, 62.3 and 52.9% respectively were due to Group A haemolytic streptococci. Of the new cases appearing in any cottage, 68% did not give rise to another case; the rest were followed by further cases ranging up to 16 in number.

Twenty-three incidents or outbreaks of sore throat were studied bacteriologically. There was no clear relation between the percentage of persons with clinical illness and the percentage shown bacteriologically to be infected. Although different serological types of streptococci were associated with different attack rates, the latter were obviously influenced by other factors. Introduction into a cottage of a sore throat due to Type 2, the most frequent type, was followed by clinical infections in an average of 36% and bacteriological infection in an average of 77% of the children in the cottage; with some other types a much smaller proportion of persons were ill than were infected. Sore throats in the children were much more often responsible for transmission of streptococcal infections than sore throats in the adults, and were more often the source of new infections than were other streptococcal lesions. Analysis showed that the types of person most often responsible for spread of infection were convalescent nasal carriers, precocious carriers, and heavy nasal carriers without symptoms. In only 2 out of 19 incidents was there any evidence to suggest that infection was being spread in the bedrooms.

Common Cold

Dr. O. M. LIDWELL described family studies on the spread of the common cold made with Dr. T. Somerville in the agricultural community of the Chalke Valley in Wiltshire. In one village of about 200 people all of the 60 or 70 households were included, weekly visits being made. The general plan was to keep records of those weeks when someone had a cold. A method of analysis was worked out which enabled estimates to be made of the relative responsibility of different classes of person—i.e., adult, schoolchild, or infant—for introducing colds into the family and of the amount of cross-infection in the family. Each family's record was divided into "incidents" comprising groups of infections possibly related, and separated from other groups by at least one clear week in which no new cases occurred. Dr. Lidwell described the method of making allowance for the chances of any person acquiring infection outside the home, and so deducing the risk of cross-infection within the family. Four different sorts of household groups were differentiated: (*a*) adults only, (*b*) adults with schoolchildren, (*c*) adults with infants, and (*d*) adults with schoolchildren and infants; further classifications depended on total numbers in the family. The most striking observation had been the experience of schoolchildren and their effect on the household. Their attack rate was about three times that of an adult living in a household without children. A household with schoolchildren suffered almost double the attack rate in its adults and infants compared with those with adults only. Infants were most highly susceptible to familial cross-infection, but their presence had little effect on the experience of the adults. Women had nearly 50% more colds than men, an observation which confirmed those made experimentally at the Medical Research Council's Cold Research Unit at Harvard Hospital. Seasonal incidence was highest at the turn of the year, and there was some suggestion of a four-week periodicity, especially in the schoolchildren and the adults living with them. Persons escaping infection from the first case in the house appeared to have an equal chance of getting it from subsequent cases. The risk of cross-infection seemed to be about one-fifth from each infected person to whom an individual was exposed.

Dr. Lidwell went on to compare these results with those of some American workers, and with preliminary results from work in progress in the North of England and among office workers in London. Where circumstances were similar there was good agreement. Differences in mode of life, such as the relative isolation of the farm labourer during his working hours, probably explained some of the variations of pattern, but many more observations were required.

Dr. H. A. CHANNON gave an account of inquiries made in the course of a study of infectious diseases in schools in Southall. During an outbreak of measles in spring, 1948, 141 of the 5–6-year-old children who caught it were visited in their homes. No connexion was apparent between the spread within the family and the type of home conditions—for example, spread among other susceptible children was the same whether they slept alone or three to a bed. Apart from the family spread, cases were traced to school contacts, but none in this series to contacts among friends in each others' homes. Among the pre-school contacts, resistance to measles infection seemed to be greater during the earliest months of life than in subsequent months.

Sonne Dysentery

Dr. C. C. SPICER, with Dr. Mair Thomas, had studied the epidemiology of Sonne dysentery, and had found that the secondary attack rate of persons exposed in their homes was considerably higher among siblings under 15 years of age than among adults. Family size had an influence on attack rate, which in families of three to four persons was one-third of that in families of five or more—due no doubt to the fact that the latter probably contained more young children. In the smaller family the secondary cases were probably infected by the initial case; in the larger ones the disease "travelled around" to a greater extent.

Dr. W. H. BRADLEY recalled the difficulties encountered 20 years ago by the epidemiologist desiring to pursue his inquiries into the home. It was encouraging to find that family investigation was now becoming easier. Commenting on the absence of any clear indication of the source of infection in some of Dr. Williams's cases, he mentioned that the possibility of milk-borne streptococcal infection should always be kept in mind; this was of course unlikely in the series under discussion, since a more widespread epidemic would probably have resulted.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Isonicotinic Hydrazide as Wonder Drug

SIR,—Through the kindness of American friends I have recently been able to make a short but intensive tour of the principal centres in the Eastern United States where the new drugs are under clinical trial. My tentative conclusions are similar to that of Dr. Peter Edwards (April 19, p. 868), "that the drug does something and may lead to something better." Not only was subjective improvement usual but cases were shown in which the miliary process was checked and, at any rate temporarily, reversed in some but not all patients; an action which hitherto had been produced by the streptomycin group alone. In cases of pulmonary tuberculosis improvement in symptoms was out of all proportion to changes in radiograph or sedimentation rate, which were negligible. Sputum conversion was exceptional, but some diminution in the Gaffky count was common in the early stages of treatment; in some cases this early reduction was followed by a rise after some weeks or months of treatment. It seems likely that proof of resistance will soon be forthcoming.

On the evidence at present available it is not justifiable to claim that these drugs are as good as chemotherapy by streptomycin and P.A.S. Clinicians are likely to have difficulty in avoiding the premature and excessive use of *iso*-nicotinic hydrazide on account of the euphoria and hearty appetite so often produced which are in contrast to the subjective effect of present-day chemotherapy on many patients. P.A.S. is a very useful drug, but its most enthusiastic advocates would hardly proclaim its virtues as an *apéritif*.

In the present state of knowledge careful study of the new drugs is urgently called for before they are widely exhibited, but there seems to be a strong case for their earlier use for patients in need of chemotherapy whose bacilli have become streptomycin-resistant.—I am, etc.,

London, W.C.1. ANDREW MORLAND.

SIR,—One might profitably augment your excellent leading article (April 19, p. 858) by the submission of a plea on behalf of such cases beyond the reach of our present-day administrative services—those of advanced and severe bilateral pulmonary disease. You mention the "hopeless" case still manifest after repeated courses of streptomycin–P.A.S. therapy. Surely there is obvious advantage to be gained by the intercession of other forms of chemotherapy between such courses as the thiosemicarbazone compounds and the hydrazides of nicotinic acid you write about, such intercessions designed to prevent the development or possible spread of resistant disease, apart of course from their immediate therapeutic value.—I am, etc.,

Tipton, Staffordshire. L. H. EUNSON.

Family Planning

SIR,—We seldom see doctors' families in which the wife accepts the full quota of pregnancies—20 or more—which Nature used so often to mete out to our grandmothers. Therefore the sentiments expressed in some letters on this subject (April 19) create somehow an impression of unreality. Whether we, the profession, are "wise" to teach poor and ignorant women how to limit their families is hardly relevant unless we arrange to ban from general use all those contraceptive appliances which we ourselves are so thankful to employ.

At a time when sociologists and psychiatrists are vociferous about the handicaps of unwanted children, it does not seem, for instance, that Dr. Carter need grieve over some of the undesired pregnancies which are lost to us through contraception. Dr. Waddy finds it a "horrible thought" that puerperal mothers should not be sent home ignorant of how to delay the next pregnancy: but it does seem that his experience of people's motives for restricting their families is drawn from unusual and highly neurotic cases. I think if Dr. Sadler would join a Family Planning Association clinic for one afternoon she would find grateful patients assuring her that their contraceptive security has done more to help the stability of family life than a whole stream of friendly enthusiasts coming to assist with their housework could ever do. Working-class mothers are not unlike middle-class mothers in their fundamental feelings.

But, to pass to wider issues, are the advocates of unlimited families for other people seriously in a position to assess their political and sociological implications? Rapidly increasing world population, in the face of world food shortages, must sooner or later lead to disaster. Surely it is for the more advanced nations to show their appreciation of such issues by setting standards for contraceptive teaching and family welfare.—I am, etc.,

London, N.W.1. JOAN MALLESON.

SIR,—The extent of the use of deliberate methods of family limitation has been fully investigated by Lewis-Faning (Papers of the Royal Commission on Population, Vol. 1), and there can be little doubt that birth control—either by appliance methods, the use of the safe period, coitus interruptus, or, in a number of unfortunate instances, by criminal or self-induced abortion—is a feature of our culture that cannot be lightly disregarded by the medical profession. It is known, moreover, that in 1947 one divorce or official separation took place for every five marriages that year. This in itself is evidence that there is, for many, much frustration and disappointment in what should be a fruitful and mutually rewarding relationship. The part played by sexual maladjustments in the generation of marital discord cannot be overlooked.

It is consequently important that those who seek advice and guidance, whether it be about intimate marital problems or about contraception, should be able to obtain it. The family doctor should in the first instance be the person responsible for this aspect of his patient's care, but he may not be able to devote to these cases the time they need. Indeed, the growth of the family planning movement may be ascribed to the fact that it fulfils a need not met by other existing services. It matters little, however, whether patients receive advice from their family doctors, at post-natal clinics, or at clinics established specially for the purpose, provided the guidance they receive is based on a full use of existing medical knowledge tempered by an appreciation of its shortcomings and of its moral and social implications.

In the Report of the Royal Commission on Population the social reasons underlying family limitation are discussed and a number of remedies suggested. These are social remedies for social causes and are beyond the powers of individual doctors to implement. This does not mean, however, that society itself may not implement them in the future.

It has been suggested that only the feckless or self-indulgent parent seeks advice about family limitation. The increasing demand for medical advice about family relationships and the spacing of children, however, probably stems from the fact that many people now recognize that getting married and rearing a family is an important job requiring knowledge and the development of appropriate skills if it is to be accomplished successfully.—I am, etc.,

Cardiff. JOYCE GRANT.

Discharge of Certified Mental Patients

SIR,—I much enjoyed the two excellent articles by Professor Alexander Kennedy on "The Psychiatric Case and the Law" (April 5, p. 754, and April 12, p. 810). There is, however, a statement in the penultimate paragraph of his second article which, as it stands, is incomplete. Under the heading "Discharge at Request of Relatives" he states, "If the patient has been detained under a reception order on petition the relative who signed the petition may, if he has become convinced that the patient should no longer be retained, ask for him to be discharged (Lunacy Act, Section 72)." This Section (72(1) of the 1890 Act) applied originally only to private patients detained on petition, but, by the National Health Service Act (1946), was extended to include Health Service patients. But the 1946 Act did not stop there. In Section 72(3) it states that in *any other case*—i.e., of patients other than private patients detained under an urgency order or a summary reception order—discharge may be effected by the appropriate relative. The appropriate relative means the nearest relative—that is, husband or wife if there is one; if not, then father; or, if there is no father, mother, and so on. The medical superintendent of the hospital may bar the discharge only in the following terms, that "the patient is dangerous and unfit to be at large."

I think that this Section 72(3) deserves mention, because it is widely used and has created an entirely new situation. It makes nonsense of the complicated machinery of certification, because the certified one can be whisked out of hospital at any time the nearest relative so desires. Much time has to be spent by the medical staff in dissuasion. The barring certificate is no real safeguard, because very few patients, once in hospital, remain for long (and the Act is worded in the present tense) dangerous *and* unfit to be at large, even if one includes "dangerous to themselves"—i.e., suicidal. In point of fact, in three and a half years I have been unable to issue a single barring certificate, although I have seen patients go out who would have been better inside. The fact is, of course, that potential danger may become actual when the patient returns once more to an environment which activated his disorder in the first place.

Section 72(3), in fact, ignores several important considerations. It does not take into account the "nuisance value" of the mentally afflicted, just one of whom can cause any amount of trouble and misery in a household, block of flats, or among the neighbours. Secondly, it is well known—and also perfectly natural—that the motives which impel the nearest relative to seek the discharge of the patient are frequently not based on an objective appraisal of his state of mind or inspired by unselfish devotion, but on such factors as emotional bias, sensitiveness to stigma, possessiveness, pangs of conscience, and pressure from the patient or other relations. The chief sufferer is apt to be the patient himself, who is removed before he has had time to recover or become stabilized, and whose symptoms in consequence often return in full force when he gets home. Although I know that some hospitals have found in Section 72(3) a useful expedient to relieve their overcrowding and dispose of cases which do not respond to special methods of treatment, I myself hold the view that the mental hospital still has and will continue to have an important twofold custodial function: to protect the mentally weaker members of society and to protect society from them.

The legal side of mental illness has now become so complicated that to scrap the lot and begin again with something very simple but effective, such as exists in Northern Ireland, might well be the best solution. In particular, it is unsatisfactory to continue to allow "the nearest relative" to be the arbiter of the patient's destiny.—I am, etc.,

Southall, Middlesex. C. R. BIRNIE.

Physiology of Sleep

SIR,—In their paper on "Studies on the Physiology of Awareness: Anoxia and the Levels of Sleep" (March 1, p. 449), Drs. J. W. Lovett Doust and Robert A. Schneider devoted considerable space to the enumeration of other concomitants of sleep and the discussion of some of them, but failed to mention those that have a direct bearing on their own findings: the marked hypoventilation of the lungs, and the resulting increase in the CO_2 content of the alveolar air and in the CO_2 tension of the blood, as well as a decrease of the *p*H of the blood. The hyposaturation of the haemoglobin of the blood fits in well with these older observations, as indices of a decreased irritability of the central nervous system, including the respiratory centre. Indeed, like Lovett Doust and Schneider with respect to the percentage of oxyhaemoglobin, the earlier workers (Bass and Herr; Endres) suggested that the increase in the CO_2 level of alveolar air be used as a measure of the depth of sleep.

Concerning the degree of anoxia reported, it is well known that a much greater hyposaturation of the oxyhaemoglobin of the blood (usually 68–75% oxyhaemoglobin, or an altitude of 17–18,000 ft.) is required to produce unconsciousness. The lowest levels of oxyhaemoglobin saturation found in deep sleep, 87–88%, will hardly produce a decrease in performance on the pursuit meter, much less an observable effect on "awareness."

With reference to Howell's vasomotor fatigue theory of sleep, the authors stated that "this theory has been criticized, but it still remains a practical possibility, for differential anoxia on a vascular basis could exist with no overall change in cerebral blood flow." Aside from the fact that the data reported by them do not point to the possible existence of a *differential* anoxia on a *vascular* basis, Howell's theory has been shown to be untenable by several investigators, most recently by Kety and his co-workers, who found that the cerebral blood flow was slightly augmented and, what is more important, there was no decrease in cerebral oxygen consumption during sleep.

It appears, then, that the reported hyposaturation of oxyhaemoglobin does not constitute a contribution to our knowledge of the "physiology of awareness" or of the *cause* of sleep, but simply complements the previously found concomitants of sleep which point to a depression of the respiratory centre in that state.—I am, etc.,

University of Chicago, Illinois. NATHANIEL KLEITMAN.

Prolonged Respiratory Paralysis after Succinylcholine

SIR,—The report of a case by Dr. J. Kennedy Harper (April 19, p. 866) will be read with interest by all those who are making use of this valuable drug. I cannot agree with the conclusions he reaches in the final paragraph.

A similar case was reported by S. H. S. Love (*Anaesthesia*, 1952, 7, 113), but "prostigmin" was not given and recovery occurred in one hour. It is at least arguable that, but for the treatment given, Dr. Kennedy Harper's case would have recovered in the same time, only 15 minutes after the end of operation.

Cases of prolonged respiratory paralysis following the use of D-tubocurarine have been described, and some authorities advocate the use of a test dose. For short cases it may be that a similar test dose is advisable with succinylcholine. Longer cases can be handled with a continuous drip, or repeated small injections of succinylcholine chloride, giving the anaesthetist a measure of control of relaxation that it is not easy to achieve with other drugs.—I am, etc.,

Hove. REX BINNING.

SIR,—In view of the fact that succinylcholine is described as an ultra-short-acting relaxant, the following case history seems worthy of record to add to the many cases now published showing its unpredictable effects (see also April 19, p. 866).

The patient was a muscular farm labourer aged 23 who was to undergo a bilateral Caldwell-Luc antrostomy. Apart from sinus infection, he appeared normal and was given as premedication "omnopon" (¼ gr. or 21 mg.) and scopolamine 1/150 gr. 40 minutes before operation. Intravenous thibpentone was given, the sleep dose being 0.4 g. Inhalation of nitrous oxide, oxygen, and "trilene" was then started, and after about two minutes it was becoming obvious that a marked excitement stage was about to occur. At this point 60 mg. of succinylcholine chloride

was given intravenously. After the usual muscular twitching complete relaxation occurred within a minute, and a full-sized cuffed Magill's tube was passed with the greatest ease. The cuff was then inflated, and, as natural respiration had ceased, intermittent positive pressure was given, using 80% nitrous oxide and 20% oxygen with no adjuvant.

The operation proceeded uneventfully, and 42 minutes later, just as the surgeon finished, the patient took his first spontaneous breath, and within a minute was moving his head and trying to expel the tube. The cuff was accordingly deflated, the tube removed, and the patient then immediately sat up and started talking rationally. He was returned to bed and suffered no ill effects.

The salient features of this case are that premedication was light, and that he had a minimal dose of thiopentone and pure nitrous oxide and oxygen after a minute amount of preliminary trilene.

It therefore seems certain that the prolonged apnoea was due to succinylcholine. I have no suggestions to make on the reason for this, but in the present state of our knowledge it must be confessed that the length of time during which this relaxant acts appears to be quite uncertain, and it is interesting to speculate on what would have happened if a succinylcholine drip had been given with the intention of maintaining a constant depth of relaxation, or if the dose recommended by the makers for a "large adult" had been used, which is 200 mg.—I am, etc.,

London, E.C.1. C. LANGTON HEWER.

Mental Disease a Symptom of Physical Defect

SIR,—Much stress has been laid of late on what is called, erroneously, I think, psychosomatic medicine, and also on the psychogenic causation of not only mental disease but also of many frank physical diseases, and it has given to many a false idea of the prominence of the mental state in the aetiology of disease.

I do not believe there is any such thing as mental disease *per se*, but that it is the symptom of a physical disease, defect, or dysfunction. The psychogenists and psychoanalysts, I know, will not agree with this view, but surely to work on the premise that one of the most obvious manifestations of a disease is the disease is similar to considering Addison's disease or jaundice from the dermatological aspect alone. To what, I wonder, would they have ascribed the cause of dementia paralytica before Noguchi demonstrated its specific cause in 1913? Would the third stage with its lalling speech have been considered to be due to an infantile fixation? I cannot follow the reasoning that it is possible to have a disease of an abstract quantity. One does not have a disease of any of the senses but rather of the organ of the particular sense, and the disease is manifest by a defect of function just as an encephalopathy or an endocrine dysfunction may cause a mental abnormality. Heredity as a cause of mental disease is universally accepted; as an abstract quality cannot be inherited of itself, surely this denotes a physical basis for mental disease?

Lest the rather fatuous criticism be levelled at me again that I am ignoring the existence of a mind, let me say that I believe the mind to be something more beautiful than the cesspool which some would have us believe it with its Oedipus and Electra complexes and the very suggestion that even the infant psyche is driven by a desire for incest and murder.

In conclusion, Sir, may I say that I agree with your leading article (November 10, 1951, p. 1136) in which you declare "psychosomatic" to be "an unnecessary term and the sooner it is dropped from the current medical literature the better"? If, however, some term be necessary in its stead, I would suggest "somatopsychic" as being more logical.—I am, etc.,

Cork. MICHAEL J. KENNEFICK.

Explosion during Anaesthesia

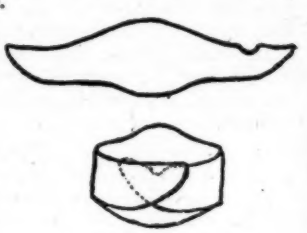
SIR,—I was interested to see Dr. G. M. Wyant (April 19, p. 870) raise the question, "What was the explosive?" in the case reported in the *Journal* of January 19 (p. 168). He suggests an explosive residue in the machine powerful enough to cause a violent explosion, occurring in this case in the patient's gullet and stomach. I submit that there is another source for the explosive—namely, the patient's bowel. I have personally witnessed the ignition of *downward* flatus by a subject (not myself) who held a lighted match close to his anus (a thin pair of cloth shorts intervening) and was able to produce flatus which ignited and burnt with a momentary blue flame, presumably the product of intestinal fermentation. I have been unable to demonstrate that such inflammable gas can be found in the stomach, but this is clearly a theoretical possibility. It is even possible that such a gas might be spontaneously combustible, as marsh gas causes the will-o'-the-wisp, and that such an occurrence might explain the recent explosion and others.

Until this matter is clarified, I think it unwise to give oxygen under pressure to relaxed patients unless through a cuffed endotracheal tube. The safe and easy method of artificial respiration by thoracic compression will suffice to carry a patient through the early stages of a modern anaesthetic without the machine being connected at all until the tube is in position.—I am, etc.,

Paignton, Devon. J. F. BURDON.

Sponge-rubber Collar for Cervical Disk Lesions

SIR,—It is generally agreed that operative measures have little place in the treatment of intervertebral disk lesions in the cervical spine. Conservative measures, however, whose aim is to provide rest and protection to the affected joints, present special difficulties in this region. The hard and unyielding nature of cervical collars made of leather or "perspex" tends to produce discomfort or pain over bony prominences. As a result, the wearers will tend to hold themselves away from contact with the collar. Thus, although the collar will prevent movements, it will often fail to give the necessary rest and support. In fact many patients will not tolerate such an appliance.



For the last few years I have been using a collar cut from sponge-rubber sheeting, ½ in. (1.25 cm.) thick. The accompanying sketch shows the shape and size of the piece required for the average case. The collar is wrapped round the neck, the ends overlapping in front, a notch being cut out of the underlap, as shown, to accommodate the thyroid cartilage and prevent discomfort in swallowing. It is held in place by a crêpe bandage or fitted with some form of buckle.

This type of collar has been found to be effective in practice and to have the following merits:

(1) There need be no delay in instituting treatment while awaiting the manufacture of a surgical appliance.

(2) It is cheap.

(3) In these days of red tape it avoids the delays involved before a general practitioner can get any surgical appliance ordered for one of his patients. He can make and fit such a collar in his own surgery in a few minutes—at least as a first-aid measure while awaiting a specialist opinion.

(4) Although it does not provide such efficient immobilization, it gives better rest and protection than a surgical appliance, for the patient can relax into it without discomfort.

(5) It is more easily tolerated for use at night.

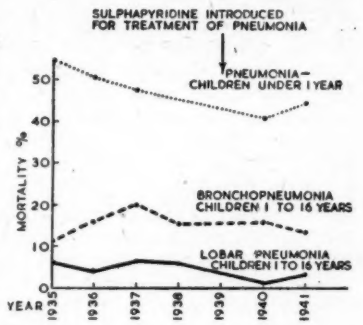
—I am, etc.,

London, S.E.1. T. T. STAMM.

Effect of Sulphonamides on Mortality

SIR,—I was very interested to read a letter entitled "Cost of Treatment" by Dr. R. McL. Todd (March 8, p. 546). During the early part of the war I was deputy medical superintendent at Alder Hey Children's Hospital, Liverpool, prior to the formation of the Liverpool University Department of Child Health, and at that time I prepared statistics

showing the mortality rate from respiratory infections before and after the introduction of chemotherapy. Sulphapyridine was introduced for the treatment of pneumonia in 1939 and the mortality rate for both lobar and bronchopneumonia in the children before and after the introduction of sulphapyridine is shown in the Graph.



It is probably unwise to draw definite conclusions from mass statistics obtained from hospital records, but one feels that the figures are of significance as the average admission of primary pneumonia to the hospital from 1935 to 1941 ranged from 1,100 to 1,200 per year. The graph suggests that the mortality rate in children with lobar pneumonia was appreciably diminished, but that there was little, if any, improvement in the mortality rate from bronchopneumonia. I found the average length of hospital treatment for primary bronchopneumonia extremely interesting:

	1935	*1941*
Children under 1 year cured in ..	25.40 days	12.05 days
„ „ „ „ died „ ..	10.48 days	4.08 days

Treatment with sulphapyridine appeared to cut short the course of the disease very considerably; at that time the children who were going to survive improved very rapidly and were probably sent out of hospital earlier than was desirable, whereas the children who died did so at a much earlier stage than they would otherwise have done with nursing treatment only.

I personally would be very interested indeed if Dr. Todd continued his carefully controlled trials of the effect of the various types of chemotherapy in the treatment of pneumonia in children, as we are ever too ready to accept new remedies without properly assessing their value.—I am, etc.,

Liverpool. ROBERT HUGHES.

Goat's Milk and Infantile Eczema

SIR,—Many doctors who have not used goat's milk instead of cow's milk in infantile eczema will have been interested in Dr. Phyllis Croft's letter (March 29, p. 709), but hopes must not be raised too high by her findings in seven cases. There is no doubt that in some cases it is of benefit, but in the majority the substitution does not improve the rash, because there are so many crossed reactions between cow and goat lactalbumin. In Hill's series (*J. Amer. med. Ass.*, 1949, **140**, 139) of 44 eczematous infants who reacted to cow lactalbumin 25 gave identical reactions to goat lactalbumin, and this appears to be the usual experience, unfortunately, in large series of cases.—I am, etc.,

Dublin. BETHEL SOLOMONS, jun.

SIR,—Dr. Phyllis C. Croft (March 29, p. 709) writes that goat's milk is definitely better than cow's milk in cases of infantile eczema.

I should like to mention a case I had in 1944. A baby boy aged 2 months was put on cow's milk; within a short period he developed an infantile eczema almost covering the whole body. I had him skin-tested (I thought it was an allergic condition), and the skin test showed a positive reaction to milk as well as fish. I thereupon put him on imported American tinned milk and the eczema almost subsided. I tried to put him on tinned milk manufactured in this country and the eczema came back worse than before. Then I tried to find out the difference between the imported tinned milk and tinned milk manufactured in this country. On close inquiry I found that the cow meal supplied by the Government to the farmers contained fish—this gave me the answer. Unfortunately, the American imported milk had to be discontinued because of lack of points—in spite of correspondence with the Ministry of Food I could not get additional points. Thereupon I got in touch with a convent not far from here, and they kindly consented to let me have goat's milk, and by special request they also agreed not to feed the goats on any form of fish or food supplied by the Government. Immediately the new diet was begun the child's eczema improved considerably. My conclusion is that it is not the milk itself but the food on which the cows are fed which brings on the eczema.

The same applies to eggs; I have done similar experiments and come to the same conclusion. Children who are sensitive to eggs often had no reactions to eggs supplied by individuals who keep their own chickens and do not give them fish.

After making further inquiries of the Ministry of Food, I have just received a leaflet stating that the form of protein they supply, and the calcium in the cow's meal and chicken food, may derive from fish, which in fact they do, hence it is the fish in the food, not the milk, that is harmful to a child with infantile eczema.—I am, etc.,

London, N.W.4. K. LINDENBAUM.

Intra-partum Uterine Rupture

SIR,—Recent correspondence in these columns on rupture of the uterus has focused some attention on the subject of rupture of the lower segment caesarean section scar discussed by us before the North of England Obstetrical and Gynaecological Society (*J. Obstet. Gynaec. Brit. Emp.*, 1951, **58**, 630). We described two cases of this abnormality, and in the subsequent discussion a number of other personal cases were reported. Dr. T. F. Redman (February 23, p. 438) mentions a further case; Dr. William Love (March 15, p. 604) adds another one. Even with the greatly reduced risk of rupture of the lower segment scar, clearly we can expect in the future that cases will appear from time to time. On this account it does not seem out of place to reiterate some of the conclusions we arrived at after considering our own cases and 66 others collected from the literature.

There are one or two important differences between rupture of the classical and lower segment scar. While the tear remains confined to the lower segment, bleeding may not be serious as the tear extends—often somewhat slowly—along the line of the avascular scar. At this time a most characteristic physical sign may appear. As the membranes bulge through the tear beneath the loose visceral peritoneum a smooth cystic swelling will appear in the lower abdomen resembling, more than anything, an over-distended bladder. It may be possible readily to palpate foetal parts across this swelling. This physical sign was evident in Dr. Love's case previously referred to. The appearance of this swelling is not a sign of impending rupture. It is a sign that rupture has already occurred. If the significance of it is not recognized and the abdomen is not opened, extension of the tear into the body of the uterus, or into the uterine vessels, or into the bladder may result in extensive bleeding and collapse of the patient. One further important physical sign is that uterine contractions persist; this may be found to be confusing.

In our opinion the most important aetiological factor is an incision, not strictly confined to the lower segment, but placed partly or completely in the body of the uterus. This is also evident in Dr. Love's case, as the incision was extended into the upper segment in the midline, making it "T"-shaped. In this respect the vertical incision has been more often to blame than the transverse one. If the more usual transverse incision is used, however, the greatest danger lies at the angles of the incision, where adequate suturing may be difficult. If we are to see this complication in the future presumably cases will conform more to this type than to our previous ideas of rupture of the classical scar.—We are, etc.,

Sheffield. C. J. DEWHURST.
H. A. ROWLEY.

SIR,—The medical memorandum by Mr. Robert Hodkinson (February 9, p. 308) was of special interest to me, as a few weeks ago I saw two cases within 24 hours of each other. Ruptured uterus is, I believe, far more common in Africa than Europe in spite of the fact that far fewer caesarean

sections are done. This frequency of uterine tears is due to the fact that patients rarely seek help in the early stages of labour. The average time in labour before admission to hospital is two to three days, and five days is not uncommon. In my two cases one was an upper segment tear and the other a lower segment. Comparison between the two shows certain points of interest.

Case 1.—Para 5, admitted to hospital after two days in labour, complaining of severe abdominal pains and pain in the shoulders: general condition poor, radial pulse impalpable, heart rate 140/min., temperature 100° F. (37.7° C.). Abdominal palpation revealed an easily felt foetus, freely movable. There were no uterine contractions, and no foetal heart sounds. In spite of the very poor condition and the lack of either blood or plasma, laparotomy was decided on, as it seemed her only chance. This was done under local field block. The foetus was lying free in the abdominal cavity and a rent was present down the left side of the upper segment of the uterus, starting just posterior to the tube. Repair was impracticable and hysterectomy was performed. A point of anaesthetic interest was that the patient, having stood laparotomy well under local analgesia, became restless during manipulation of the uterus, but perfect operating conditions were obtained after giving as little as 3 ml. 10% hexobarbitone. She left the theatre in rather better condition that she entered it and made an uneventful recovery.

Case 2.—Para 6, admitted to hospital after three days in labour, complaining of severe abdominal pain: general condition fairly good, pulse 120/min., moderate volume. Abdominal palpation revealed an easily felt foetus with head not engaged. There were no uterine contractions. Laparotomy was again performed under local analgesia and again a minute dose of hexobarbitone produced satisfactory conditions later in the operation. The foetus was lying free in the abdomen and the tear was centrally placed in the lower segment, running vertically downwards into the cervix. Hysterectomy was more difficult in this case as the tear ran past the line of severance of the hysterectomy, and one had to get very low down to suture it and stop the bleeding. Convalescence was stormy and a pelvic infection developed, presumably due to an ascending infection from the torn cervix. However, at the time of writing she is almost ready for discharge.

I would thus like to add to Mr. Hodkinson's list of reasons why spontaneous lower segment ruptures are more serious than upper segment. First, they are more difficult to deal with, and, secondly, there is the risk of infection if the cervix is involved.

I have to thank Dr. R. L. Cheverton, Director of Medical Services, Gold Coast, for permission to submit this letter.—I am, etc.,

Winneba, Gold Coast. D. B. SCOTT.

Damnable Heresy?

SIR,—As a member of a council of a university college which as yet has no medical school, I was recently sent a copy of the interim report of the University Grants Committee for the years 1947–51 on University Development. Although it was no concern of mine officially, one of the first things I looked at was the section on earmarked recurrent grants for medical education, and I was horrified to read the following:

> In particular the Committee laid great stress upon the need for placing all clinical departments of a medical school in the charge of whole-time professors appointed and paid by the university, who would receive salaries of such amounts that they would not need to supplement them by outside earnings: it was a corollary of this that suitable numbers of full-time readers and lecturers should be appointed, from among whom the professors of the future might be expected to be recruited.

What damnable heresy is this? Are future medical students to be instructed in their art by those who have never been inside the house of a sick person? Will it be possible to become a professor of obstetrics without having delivered a baby in a private house? Will students learn paediatrics from one who has never seen the appalling difficulties of the working-class mother trying to rear a baby in one room in a condemned slum? Will they learn their medicine from one who is more concerned with the state of the patient's intracellular electrolytes than whether he has slept well or had his bowels opened that morning?

Undoubtedly there is a place for whole-time teachers. Many of them are doing excellent work, but so far they have nearly all graduated in private practice, and surely most clinical teaching is best done by those who spend or have spent some of their time in treating patients in their homes or in the intimate atmosphere of the consulting-room. I remember that during the latter part of the war, when discussion groups were held about the future medical service, it was recommended that all would-be consultants should spend some years in general practice. Most regrettably this has been completely abandoned. A new consultant has merely to pass through the stages of house-officer, registrar, and senior registrar before having to deal with the human problems of patients referred to him. At present, however, he has had the advantage of having been instructed by those experienced in these things. In future it will be possible for him to have served only under those who have been whole-timers from their professional infancy, and who in some cases seem to rejoice in treating patients with coldness and the family doctor with rudeness.—I am, etc.,

Leicester. J. VERNON BRAITHWAITE.

Streptomycin in the Tuberculous Knee-joint

SIR,—The paper by Dr. R. T. Ahern and Mr. G. P. Arden on intra-articular streptomycin in tuberculosis of the knee (March 1, p. 466) is only an interim report, but I feel bound to accept with considerable scepticism their statement that their results are encouraging.

All will agree that early diagnosis is essential and that biopsy of the joint or a regional lymphatic gland should be carried out more frequently to obtain this information. The authors report 10 cases of tuberculous infection of the knee, yet in only five of these was a biopsy carried out and in these cases alone was the diagnosis of tuberculosis proved. Of those five cases in which the infection was proved, two came to arthrodesis, one started and ended treatment with only 10 degrees movement, one started treatment with 90 degrees movement but the final range is not stated, and one had almost full movement at the start of treatment and full movement 19 months after this was completed.

I do not wish to deprecate the use of new methods in treatment, but this report does not appear to show any advance over the more usual methods of immobilization with or without systemic streptomycin in those cases quoted of proved tuberculous disease of the knee.—I am, etc.,

Stanmore. JOHN A. CHOLMELEY.

Mr. Bevan

SIR,—I am not a supporter of Mr. Bevan or of the Labour Party, but I should like to support Dr. Eric Townsend's comments (April 19, p. 870) upon your leading article (April 5, p. 749) on "Bevan's Book." I feel that the writer was extremely partisan and that the article was to the discredit of the *Journal*.—I am, etc.,

Thornton Heath, Surrey. W. M. MAXWELL.

Fouling the Nest

SIR,—The standing of the medical profession in the eyes of the public must obviously be affected by the low opinion of their colleagues so often publicly expressed by distinguished medical men. The layman is given a picture of an average general practitioner too incompetent to handle his surgery and too cowardly to refuse an unneeded prescription for fear of losing 17s. 6d. per annum.

I do not believe this is a true picture. In a long career I have met professional and business men in many spheres, but only among doctors have I found this almost pathological indulgence in virulent criticism of their fellows. Lawyers, architects, accountants, engineers have, of course, their differences, but they do not bring their professions into disrepute in the public eye. Is it an occupational disease of doctors?—I am, etc.,

London, S.W.1. COLIN HURRY.

POINTS FROM LETTERS

Medical Aspects of Tobacco-smoking

Dr. P. P. TURNER (Enfield, Middlesex) writes: The paper by Dr. R. Bodley Scott (March 29, p. 671) made interesting reading, but I feel impelled to point out that C. S. Calverley made no contention that:

"... they who use fusees
All grow by slow degrees," etc.

The line preceding this reads: "Doctors have said it."

Johann Mikulicz-Radecki

Mr. V. J. KINSELLA (Sydney, Australia) writes: In the latter part of 1950 an interesting but inconclusive correspondence appeared in your journal in regard to the nationality of Johann Mikulicz-Radecki. He was described as a German, then as a Pole, and then as an Austrian. No doubt, even at this late stage, the opinion of his chief, Billroth, would be of interest. To-day, while browsing through Billroth's letters, I found one written on September 7, 1881 (the year of his first gastrectomy), to an ex-pupil, Czerny. Billroth refers to the outstanding progress made by his assistants, Wölfler and Mikulicz, so that he, Billroth, becomes almost superfluous in his own clinic. "Mikulicz is now leaving, because he has married, and he goes, with my consent, to the Poliklinik, as *Privat-dozent*, if nothing eventuates about Cracow. He is by birth a Pole, and would well be able to lecture in Polish; but, with me, he has become too German, and I fear that will make him impossible for Cracow. ... Wölfler and Mikulicz have made the Clinic so comfortable for me, especially in operating, that I feel it has made me lazy; I must now pull myself together again." (*Briefe von Theodor Billroth*, 8th edition, Hanover and Leipzig, 1910, p. 224.)

Mental Health Research Fund

Dr. J. M. ALSTON (London, W.1) writes: In your leading article (March 29, p. 699) a conference on research in mental health is described in considerable detail. Many untried or unsuccessful methods of investigation were mentioned, but nothing was said about the many forms of physical disease which cause mental disturbance. ... These detectable agencies cause almost every known form of mental derangement, and it would seem a first duty to understand intimately how they produce these effects. In a book published recently (*New Outlook on Mental Diseases*, by F. A. Pickworth; Bristol, John Wright and Sons) the author produces evidence pointing to a solution of this problem. ... The various specialists at the conference seemed unable to focus on *aberrations* of mental function (which cost us £100m. a year) without explaining normal mental function at the same time. It is as if no one would investigate urinary diseases until the process of unravelling the physiology of the kidney had been completed to philosophical satisfaction.

Foreign Body in the Eye

Mr. I. J. GOOD writes: Recently a speck of dust settled on my eyeball, and washing the eye had no effect. The particle adhered obstinately to a particular point on the eyeball. I eventually removed it by means of a hair extracted from my eyebrow. Holding the root between finger and thumb, I placed the thin end of the hair horizontally against the eyeball, above the particle. On closing the eyelid the particle was at once pushed down and was easily removed.

Mr. J. E. LIDDIATT writes: Some years ago, while having a tooth stopped by my dentist, I took up his little dentists' mirror and was astounded to observe how it magnified every detail, and would obviously permit me to remove any eyelash, or foreign body, that might get into the eye. ... I have since bought nearly a thousand, and I am continually receiving letters from people to whom I have given them, saying how useful and wonderful they have been in cases of emergency.

Infective Gangrene of the Mouth

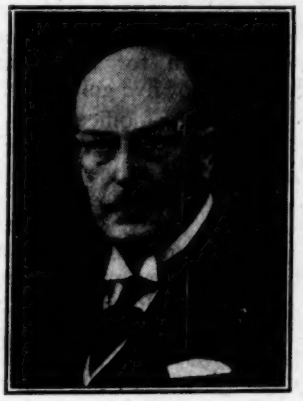
Dr. J. O. SHIRCORE (Nyasaland) writes: With reference to Dr. Frank Marsh's letter (February 23, p. 439) commenting on your report of Dr. D. V. Jelliffe's paper read at the Royal Society of Tropical Medicine in which the latter spoke of a form of infective gangrene of the mouth which differs from cancrum oris since it affects the bones (January 26, p. 198), it might be of interest to draw attention to a short paper by the writer, entitled "A Note on Cancrum Oris and its Treatment with Antimony Arsanilate," published in the *East African Medical Journal* of May, 1947. ... It would appear that the epidemiological factors under which the cases described here arose were similar in each case and, as 50% showed also bone lesions, in my view whether or not the destructive process extends to the bone depends on the degree of malnutrition and avitaminosis of the patient.

Obituary

Sir MILSOM REES, G.C.V.O., D.Sc., F.R.C.S.Ed.

Sir Milsom Rees, who died at his home at Broadstairs on April 23 at the age of 86, was laryngologist to King George V during the whole twenty-six years of his reign, and to Queen Mary and the Royal Household, and also to the late Queen Alexandra and the late Queen of Norway. He was a remarkable man, adventurous in mind and body, and he spread his energies over a very wide field, not limited to medicine, and some of his interests were quite unexpected.

John Milsom Rees was born on April 20, 1866, the son of John Rees, of Neath, Glamorgan, and received his medical training at St. Bartholomew's, London, qualifying in 1889. He served as resident medical officer at the Golden Square Hospital for Diseases of the Throat and as senior resident medical officer at the North West London Hospital. Directing his attention to laryngology, he took the F.R.C.S.Ed. in 1892 and obtained the appointment of surgeon to the ear, nose, and throat department of the Prince of Wales's General Hospital, Tottenham. In his consulting practice in Upper Wimpole Street he soon had among his patients prominent singers and speakers, and often enabled them to make a public appearance which otherwise would have been impossible. He made a special study of the vocal cords —he always spelled them "chords"—in singing and public speech, and he could tell many interesting stories of famous stars of the operatic firmament upon whom emergency treatment was necessary. Singers are traditionally temperamental, and sometimes the laryngologist had to be a psychologist and diplomatist in addition. Milsom Rees more than once saved the situation in Covent Garden. He was laryngologist to the Royal Opera House and to the Guildhall School of Music, and he was made an honorary freeman of the Worshipful Company of Musicians. He could have written a book on this side of his professional experience alone. He had attended Melba and also Patti, although Patti had almost ceased her public appearances by the time he entered practice. His admiration for the quality of these and other famous voices was almost devout.



Music, however, was only one of his interests. He was a great sportsman, and from the relatively quiet fields of cricket, football, and boxing in South Wales in his early days he went out to find fresh worlds to conquer in Central and East Africa, the Sudan, and Madagascar, where he pursued big game. He was proud to hold a world record for killing a mad buffalo which, it was said, had accounted for the deaths of over twenty people. But his experience in the wilds of Africa was not confined to game or to emergency operations on local notables. On his suggestion to the Governor of Tanganyika a hospital was built at Arusha. It was certainly needed, for there was no other hospital

nearer than Nairobi, two hundred miles away. The hospital was built, Rees himself subscribing half the cost. He also purchased a coffee estate of 5,000 acres in this region, on which he spent a very large sum of money, and later he bought four other estates a few miles away, all of which became highly successful. Another venture of his in the same connexion was the purchase of the Nyanza salt mines in 1926. At that time they were in a very bad way. Under the expert management of his co-director they were converted into a very successful and well-equipped modern concern.

A year or two after his African exploits he was winning trophies on the golf course. In 1927 he won a cup presented to the British Senior Golfers' Society by the United States and Canadian Senior teams on the occasion of the first international meeting, and tied for the same event three years later, but was beaten on the play-off. He made a number of golfing records both at Walton Heath and on the course at Lake Como; his enthusiasm for the game was such that he was a member of five golf clubs.

The list of offices held by Milsom Rees at one time or another, and generally for a long time, is a remarkable tribute to the range of his interests. The hospitals of which he was vice-president or governor included Charing Cross, King George V, the West End Hospital for Nervous Diseases, London Hospital, London Jewish Hospital, National Hospital for Diseases of the Heart, Middlesex Hospital, St. Mary's, and the Royal Free. He was a governor of the University of Wales and Monmouthshire, of Epsom College, of the Royal Surgical Aid Society, of the Bethlem Royal Hospital, and of the Medical College of St. Bartholomew's, in which last hospital the Milsom Rees operating theatre is a memorial of his association with the institution, dating from his student days. He was also a vice-president of the People's League of Health, first honorary member of the Rahere Society (in honour of the founder of the priory of St. Bartholomew), a member of the Medical Advisory Committee of the Nuffield Provincial Hospital Trust, of the governing body of the British Postgraduate Medical School, of the Central Appeals Committee of the B.B.C., of the council of the National Association for the Prevention of Tuberculosis, of the committee of the Rheumatism Clinic in Peto Place, and of the council of King Edward's Hospital Fund for London. The British Red Cross Society and the Order of St. John also claimed his interest. With such commitments it is not to be wondered at that he did not write much, even on his chosen specialty, but in 1937 he published a work on the care of the vocal cords in singers and speakers, and in 1938 another on practical hints on singing in preparatory schools. One of his last public appearances was in 1941 in the Section of Otology of the Royal Society of Medicine, when he addressed the members on the role of the labyrinth in man and animals. Honorary offices which he held in addition to those already mentioned were those of laryngologist and aurist to the Musicians' Benevolent Fund and surgeon to the Sussex Throat and Ear Hospital, Brighton.

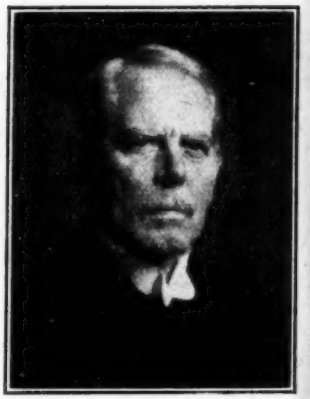
Until recent years Sir Milsom Rees enjoyed abundant health. He was accustomed to attribute it to the fact that he had been practically a teetotaller and non-smoker all his life, this notwithstanding the fact that his best friend, the late Alfred de Rothschild, who made him a trustee of his residual estate, and who possessed the best wines in France, sent him ample supplies, which enabled him to dispense a choice hospitality while himself abstaining. In 1939, however, he sustained a severe accident, with bad laceration of the head and face. From this he recovered, but a few years later a serious illness developed, and for some time he had been living in retirement at Broadstairs, in a house which he had named Arusha after his African experiences.

He was made C.V.O. in 1911, a knight in 1916, K.C.V.O. in 1923, and G.C.V.O. in 1934. Edinburgh conferred on him its honorary D.Sc. He married in 1894 Eleanor Jessie, daughter of the late William P. Jones, of Finchley, and had a son and a daughter.

Sir DAVID WALLACE, K.B.E., C.M.G., LL.D., F.R.C.S.Ed.

A long life as a surgeon ended with the death in Edinburgh of Sir David Wallace on April 21, within a few months of his 90th birthday.

David Wallace, who came of a Fife family, was born in July, 1862, the son of Mr. David Wallace, of Balgrummo, and was educated at Dollar Academy and at the University of Edinburgh, where he graduated M.B., C.M. in 1884. He then held a demonstratorship in the anatomy department, the recognized approach to a surgical career, and obtained the further qualifications of M.R.C.S. in 1886 and F.R.C.S.Ed. in 1887. He was appointed assistant surgeon to Edinburgh Royal Infirmary in 1892 and was full surgeon from 1908 to 1923, when he became consulting surgeon. While he remained an excellent general surgeon, his great interest lay in urology, in which he was one of the pioneers in Edinburgh. He was the author of many articles in the medical journals. In 1900 he served in the South African War as surgeon in charge of the Edinburgh South African Hospital. For his services he was mentioned in dispatches, received the medal and clasp, and, shortly after his return to Edinburgh, was appointed C.M.G.



[*Drummond Young, Edinburgh*

In 1908 Sir David Wallace played an important part in the formation of the Edinburgh branch of the British Red Cross Society and was its honorary secretary or chairman for more than 30 years. Although a Territorial officer in the R.A.M.C., during the war of 1914–18 he was seconded for duty with the Red Cross and was the commissioner of the south-eastern area of Scotland. During the war many large houses were generously offered for use as convalescent homes, and the smooth working of this scheme owed much to the tact with which Sir David Wallace handled difficult situations without giving offence to the owners, whose wishes in the way the properties should be used did not always fit in with official requirements. He retired from the Army with the rank of brevet lieutenant-colonel. For his services he was appointed C.B.E. in 1918 and K.B.E. in 1920. About the same time he was appointed Deputy Lieutenant of the City of Edinburgh. In 1930 the University of Edinburgh conferred upon him the honorary degree of LL.D.

After leaving the Infirmary Sir David Wallace was for many years surgeon to the Royal Edinburgh Hospital for Incurables and a member of the council of the V.A.D. At an earlier date he was examiner in surgery and clinical surgery for the University of Aberdeen. He was President of the Royal College of Surgeons of Edinburgh from 1921 to 1923 and at the time of his death he was its senior resident Fellow. He was also honoured by election to the French Association of Urology. Sir David Wallace, who was an excellent teacher and popular with students and colleagues alike, always had a large class in clinical surgery at Edinburgh Royal Infirmary.

Although an angler, a golfer, and a curler, his main outdoor recreation was shooting—during his summer holidays, usually in the Orkneys, and in winter, when work permitted, in the neighbourhood of Edinburgh.

Sir David Wallace is survived by his wife, who is a daughter of the late Sir Thomas Clouston, the eminent mental specialist, and by his two sons. Lady Wallace, who was appointed C.B.E. in 1946, is well known for her work on behalf of the Victoria League and the Queen's Institute of District Nursing.—W. J. S.

G. B. FLEMING, M.B.E., M.D., LL.D., F.R.C.P. F.R.F.P.S.

Professor G. B. Fleming, emeritus professor of medical paediatrics in the University of Glasgow, died in Glasgow on April 16, at the age of 70. His death has brought to a close a span of three generations of family practice in Glasgow. His grandfather qualified in medicine in 1830 and his father in 1872 and both were surgeons at the Royal Infirmary, his father being a contemporary of Lord Lister.

Geoffrey Balmanno Fleming was born on February 20, 1882, and was educated at Haileybury, King's College, Cambridge, and at the University of Glasgow, graduating B.Chir. in 1908 and taking the Cambridge M.B. in 1910. He proceeded M.D. in 1914. After resident posts at the Western Infirmary and Ruchill Fever Hospital and a period of postgraduate study in Vienna, he became assistant to the professor of medicine at Anderson's College. During the war of 1914–18 he served in the R.A.M.C. in East Africa, retiring in 1919 with the rank of lieutenant-colonel. For his services he was mentioned in dispatches and appointed M.B.E. On his return to civilian life he became interested in paediatrics and for a period of 35 years he served on the staff of the Royal Hospital for Sick Children, Yorkhill. In 1930 he was appointed to the chair of medical paediatrics in the University, after having been Gow lecturer in medical diseases of infancy and childhood since 1924. He retired in 1947. Under his guidance paediatrics assumed a new importance for the medical student. Tuition had already been made compulsory, but the time allotted to teaching was increased, and in 1935 it became a part of the final examination in medicine.

Fleming was a frequent contributor to medical journals, and in the period of his most active research, immediately after his return from service in the war of 1914–18, devised his own apparatus for the estimation of basal metabolic rates in small infants, using the results to calculate the caloric requirements of infants of various ages. Indeed, he can be regarded as one of the pioneers in this work and earned for himself a great reputation both at home and abroad. In his later years he became very active in administration and committee work. He was president of the British Paediatric Association in 1946 and from 1946 to 1948 was president of the Royal Faculty of Physicians and Surgeons of Glasgow, an honour which had been conferred on his grandfather before him. He retained until the end his interest in the Faculty and in the part it could play in shaping the medicine of the future. When the Faculty celebrated its 350th anniversary in 1949 he was elected an Honorary Fellow, and in the previous year he received the honorary degree of LL.D. of the University of Glasgow. In 1947 he was elected a Fellow of the Royal College of Physicians of London. Fleming served on three occasions as an officer of the Section of Diseases of Children of the British Medical Association. At the Glasgow meeting in 1922 he was one of the honorary secretaries; in 1926 (Nottingham) he was a vice-president; and when the Association met at Aberdeen in 1939 he was president of the Section.

All who knew Fleming were impressed by his integrity and honesty. Although at times he might have given the impression of being a little aloof, to work with him was to grow more and more fond of him. He had an inborn courtesy which belonged to an earlier age and he was never heard to speak ill of a colleague. He had many interests outside the field of medicine. He was a good shot, an enthusiastic angler, and he played golf regularly. He loved, perhaps best of all, the company of congenial friends, and his generous hospitality in his own home was reminiscent of the Edwardian age. His health broke down last September and he faced the pain and discomfort of his long illness with simple faith and courage. He was unmarried.—S. G. G.

W. W. G. writes: May I add a further short tribute to the late Professor G. B. Fleming? I first knew him in my student days when he taught in the wards of the Western Infirmary. Later I was his junior colleague on the staff of the Royal Hospital for Sick Children, and for the past decade I had the privilege of working in the closest co-operation with him on the council of the Royal Faculty of Physicians and Surgeons and throughout his tenure of office as president of that ancient corporation. Professor Fleming belonged to one of the oldest Glasgow families; he was a burgess of the city, as had been his forebears through 14 generations in direct line. Fleming was a man of the very highest principles. Blessed by ample private means, he did not consider that it was right that he should accept payment for any services, and in fact in the days of the voluntary hospitals he made large contributions not only to the institute with which he was connected but to every good cause. To the Royal Faculty he was a generous benefactor, and indeed only a few days before his death he acquired and presented to it a notable portrait of its founder, King James VI of Scotland and I of England. In addition he presented a large sum of money to inaugurate a fund for the furtherance of postgraduate medical education. The Royal Faculty of Physicians and Surgeons has been blessed by many outstanding men who have occupied its presidential chair, and Fleming must be regarded as among the greatest of these. His counsel and judgment were of inestimable value, and he was ever ready to give his time without stint. He became the ideal "elder statesman," and his passing is a grievous blow which will be felt in Glasgow and the West of Scotland. His name will live in the annals of the Royal Faculty of Physicians and Surgeons.

With the death on April 6 of Dr. R. J. MILLS at the age of 96 the medical profession loses one of its oldest practising members. He relinquished National Health Service work in the autumn of 1951, but continued in private practice almost to the time of his death. Robert James Mills was

born at Norwich in 1856, the son of Mr. Jacob Mills, a partner in a firm of corn merchants and maltsters. At the age of 16 he was apprenticed to a local medical practitioner, Mr. W. H. Day, whose great-nephew, Dr. George Day, is now in practice in the city. For two years or so he gained an insight into the life of a doctor, working also in the Norfolk and Norwich Hospital as a pupil and dresser. Dr. Mills qualified before he was 21, being admitted a Licentiate of the Society of Apothecaries of London, a Member of the Royal College of Surgeons of England, as well as obtaining the degrees of M.B., C.M. of the University of Aberdeen, all in the year 1876. After qualifying he became a ship surgeon and visited India. When he returned to this country he went into practice in Norwich, and almost immediately was selected for the position of police surgeon, a post he held for 60 years, from 1877 (when he was still only 21) to 1937. Dr. Mills was specially interested in skin diseases, and he paid many visits to the Continent, where he met some of the great nineteenth-century workers in science, including Pasteur, Finsen, and Röntgen. He was one of the first to see the possibilities of treating skin diseases by *x* rays, and before the end of the nineteenth century he had set up his own *x*-ray clinic in Norwich. Dr. Mills is survived by his wife and one married daughter.

By the death of Dr. JOHN HOWARD-JONES, at the age of 86, the county borough of Newport, Monmouthshire, has lost a great friend and benefactor. For 33 years, from 1899 to 1932, as medical officer of health, he played a prominent part in the life of the borough. He was born at Llanwrda, Newcastle Emlyn, in 1866, one of a family of 14, most of whom entered the Church or the medical profession. One brother, the Reverend E. Griffiths Jones, became principal of Bradford Theological College. After leaving the Normal College, Swansea, John Howard-Jones entered Edinburgh University to study medicine, graduating M.B., C.M. in 1890, and proceeding M.D. in 1899. Meanwhile he had taken the B.Sc. in 1892 and the D.Sc. in public health a year later. After holding the post of assistant demonstrator of pathology in the University of Edinburgh he became assistant surgeon to the Dowlais Iron Company, a post which he held for a number of years before he was appointed to be medical officer of health and port medical officer of Newport. He was also superintendent of the infectious diseases hospital there and police surgeon. The health services of Newport were an absorbing interest to Dr. Howard-Jones, and although his activities were directed in the main towards their improvement he became a stalwart champion of the welfare of seamen. His efforts to better conditions in the forecastle were unceasing, and his contributions on this subject to the *Journal of the Royal Sanitary Institute* focused attention upon the existing evils. At the International Congress of Hygiene at Antwerp in 1913 he read a paper entitled "The Necessity for an International Standard of Hygiene in Crews' Quarters." There is no doubt that his pioneer work for seamen's welfare has borne fruit and will remain a permanent memorial to his efforts. Dr. Howard-Jones was associated with the old Volunteers, which he joined in 1897, and he was a keen Territorial. During the first world war he served as a lieutenant-colonel with the Welsh field ambulance unit. He was awarded the Territorial Decoration. His work for the public health service was recognized by his election to the presidency of the Society of Medical Officers of Health in 1928. He was also an examiner for the Royal Sanitary Institute, and he served on a number of committees of the British Medical Association. His retirement from the post of medical officer of health did not terminate his activities, for his natural vigour of mind and body would not allow him to remain inactive for long. He undertook a voyage as ship surgeon, and later, at the age of 72, he served his country in the second world war by taking the place of a younger colleague as medical officer of the Newport Shipping Federation. He is survived by his wife, one son, and two daughters.—D. E. L.

Medical Notes in Parliament

HEALTH SERVICE BILL (continued)

Colliery Medical Services

On April 23, after prolonged debate, the House of Commons set up a time-table for the National Health Service Bill. One day was allotted to the remainder of the committee stage of the Bill. This was resumed on April 24.

On Clause 1 (charges for certain drugs, medicines, and appliances) Mr. J. D. MURRAY moved an amendment to provide that no charges should be made in respect of services to a patient at a colliery medical centre. Such centres were provided by the Miners' Welfare Commission. He asked the Minister for an assurance that if a workman received an injury in or about a mine and attended a colliery medical centre, but not a hospital, he could receive a truss, an elastic stocking, bandage, or knee-cap free of charge.

Mr. HARRY CROOKSHANK said that Clause 1 referred only to hospital and specialist services which came within the National Health Service. Anything outside that service was not affected in any way by the Bill. Therefore, anything which went on in colliery medical centres would not be affected by the Bill. The amendment was withdrawn.

Mr. HECTOR MCNEIL moved to insert a provision that no person receiving benefit or a dependant of a person receiving benefit under the National Insurance Acts should be charged for services under the Bill.

Miss P. HORNSBY-SMITH said those who suffered industrial injuries already drew higher benefits than the ordinary sick or disabled who might be suffering the same hardship or pain. To make a dispensation in regard to those who drew higher benefits was not justified and the Government could not accept the amendment. The amendment was then negatived without a division.

Clause 1 was then approved by 305 to 285.

Teeth

On Clause 2 (charges for dental treatment) Mr. CROOKSHANK moved amendments to exclude from any charge the clinical examination which a patient might have, and the report on it. The House agreed to the amendment. An amendment was accepted at the suggestion of Mr. IAIN MACLEOD to omit from the proposed charge work done by a dentist to arrest bleeding. This amendment deleted the qualifying phrase "caused by the extraction of teeth." The House accepted the amendment.

Mr. HILARY MARQUAND moved to exempt from all charge any service for which the current authorized fee was not more than £1. Mr. J. BAIRD said the dental service was running very well, but if the charge Mr. Marquand proposed to omit was imposed they would go back to the early days of the service when there were complaints of unethical conduct by dentists. Emergency treatment of all kinds would be performed outside the National Health scheme.

Mr. SOMERVILLE HASTINGS contended that the proposed charges would prevent people seeking dental treatment as soon as they should. Mr. CROOKSHANK said that if the amendment were adopted the greater part of the savings estimated under the Bill would be lost. He recommended the Committee not to accept the amendment.

Mr. W. ROSS pointed out that the charges on dentures which had reduced expenditure for that purpose by the Scottish Department from just over 60% of total expenditure to 30% had not reduced the number of dentists in the general dental service. It had actually increased this total.

The words proposed to be inserted in the clause were then rejected by 303 to 283. On the motion of Mr. Crookshank, the age of exemption from these charges for young persons was raised from 16 to 21, and Clause 2, as amended, was approved by 298 to 284.

On Clause 3 (power to vary or abolish certain charges) Sir EDWARD BOYLE moved to amend the power to vary a

maximum charge by Order in Council by substituting the word "lessen" for the word "vary." Mr. Crookshank accepted the amendment.

Disciplinary Powers

On the motion that Clause 5 (evasion of charges) stand part of the Bill, Mr. JOHN WHEATLEY said the clause introduced something new into the National Health Service by imposing penal provisions against people who came under the Service.

Mr. CROOKSHANK said the Government endeavoured to make collection of charges simple by merely having people make a declaration. If they were beneficiaries under the National Assistance Board all they had to do was to produce the books. If dishonest people used another person's book some effective punishment should be provided. It would not be an offence to produce a book on behalf of a neighbour or friend, nor to take a receipt for one. If a person knowingly represented himself to be someone else or if a woman falsely represented that she had borne a child within the previous twelve months and so got dental treatment for nothing, that would be an offence. The clause was added to the Bill by 293 to 274. On the motion of Mr. JAMES STUART a new clause was added empowering the remission of charges for dentures supplied by teaching hospitals. This completed the committee stage. The report stage and third reading were set down for May 1.

Stage Hypnotism

The Hypnotism Bill was read a second time without debate in the House of Commons on April 25.

Rejected Recruits.—About 17% of National Service recruits are rejected for reasons of health, and about 18% of class G and class Z reservists.

Medico-Legal

ROYAL COLLEGE A "CHARITY"

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In 1950 Mr. Justice Danckwerts decided[1] on a motion by the trustee of Lady Bland-Sutton's will that the Middlesex Hospital Medical School had not passed into public ownership, and that the Royal College of Surgeons was in law a "charity," because its real object was the promotion and encouragement of the art and science of surgery and not the interests of surgeons. Last year the Court of Appeal overruled[2] Mr. Justice Danckwerts on both points, and ruled that they were bound by a decision of the Court in 1899[3] to hold that the College was not a "charity": they thought there was no evidence that its purpose of furthering the professional interests of surgeons was not merely ancillary to its object of furthering the art and science of surgery.

From this judgment the College appealed to the House of Lords, and their Lordships by a majority of four to one decided on April 3[4] that Mr. Justice Danckwerts had been right, the Court of Appeal had been wrong, and that the College is in law a "charity." Unless Parliament takes a hand this decision is final and conclusive.

Lord Morton of Henryton said that it was regrettable that in order to find out what was or was not a charity according to English Law it was still necessary to refer to the preamble of a Statute of Queen Elizabeth I, which was not passed for the purpose of defining "charity" but for the reformation of certain abuses, and the whole of the Statute except the preamble had been repealed. He said that after considering the charter granted by King George III on the establishment of the College in 1800 he had no doubt that the object of the College was "the due promotion and encouragement of the study and practice of the art and science of surgery." "Study" embodied the idea of research in the laboratory, "practice" that practical experience which can be gained only by using surgical instruments on human or other bodies. There was no statement in the charter or elsewhere that one of the objects of the College was to be the promotion of the interests of individuals who were carrying on their profession as surgeons. He did not think the Court of Appeal in the 1899 case had been right in thinking that the promotion of the interests of practising surgeons was one of the main objects of the College.

In his dissenting opinion Lord Cohen said that the predecessors in title of the College appeared from the recitals of the charter of 1800 to have been in the nature of trade guilds, none of whom could have claimed that their non-charitable activities were merely ancillary to a main object which was charitable. It was to be noted that the master of the College and the governors and court of assistants had power to make and had made by-laws for the protection and defence of members of the College and the removal of those found guilty of professional misconduct. In his view the "defence" activities of the College were not purely ancillary to its main charitable object, and he would have upheld the Court of Appeal's decision.

[1] *British Medical Journal*, 1950, 2, 685.
[2] Ibid., 1951, 1, 533.
[3] *In re Royal College of Surgeons* [1899] 1 Q.B. 871.
[4] *The Times*, April 4.

Universities and Colleges

UNIVERSITY OF LONDON

Franz Bergel, D.Sc., Ph.D., has been appointed to the University Chair of Chemistry, tenable at the Institute of Cancer Research, from April 1, in succession to the late Professor G. A. R. Kon, F.R.S.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE CERTIFICATE IN PUBLIC HEALTH.—P. A. Allsopp, C. H. J. Baker, Z. El. A. Ibrahim, V. S. Krishnaswamy, D. K. MacTaggart, V. Poonoosamy, A. G. Poulsen-Hansen.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

Election of Fellows

At a quarterly comitia of the College held on April 24, with the President, Sir Russell Brain, in the chair, the following were elected Fellows of the College: R. H. Quentin-Baxter, M.B. (New Zealand); H. W. Wunderly, M.D. (Australia); F. C. O. Valentine, M.R.C.P. (London); I. McD. Allen, M.D. (New Zealand); Doris M. Baker, M.D. (London); C. C. Chesterman, M.D. (London); J. R. Blaze, M.D. (Ceylon); A. S. Hall, M.B. (Bucks); G. Victoria Smallpeice, M.D. (Oxford); P. B. Fernando, M.D. (Ceylon); R. W. Luxton, M.D. (Manchester); H. L. Hoffman, M.D. (Bath); N. F. Maclagan, M.D. (London); Lieutenant-Colonel S. M. K. Mallick, M.B. (Lahore); T. A. Lloyd-Davies, M.D. (Notts); E. G. Brewis, M.D. (Newcastle); T. E. Lowe, M.D. (Australia); T. N. Fraser, M.D. (Glasgow); The Hon. W. S. Maclay, M.D. (Berks); O. H. J. Maxwell Telling, D.M. (Leeds); D. M. T. Gairdner, D.M. (Cambridge); M. Gelfand, M.D. (Southern Rhodesia); D. A. K. Black, M.D. (Manchester); G. A. Smart, M.D. (Newcastle); I. Muende, M.B. (London); R. C. MacKeith, D.M. (London); H. A. Burt, M.B. (London); R. A. J. Asher, M.D. (London); Frances V. Gardner, M.D. (London); A. C. Frazer, M.D. (Birmingham); D. W. Smithers, M.D. (London); K. W. Donald, M.D. (Birmingham); A. H. T. Robb-Smith, M.D. (Oxford); Air Commodore C. A. Rumball, M.R.C.P. (London); A. Bedri, M.B.E. (Sudan); Sir Rudolph A. Peters, M.D. (Oxford).

The President presented the Conway Evans Prizes to Sir Gordon Holmes, F.R.S., for his contribution to British neurology and to Professor S. P. Bedson, F.R.S., for his researches into the bacteriology of viruses. The awards were made jointly with the President of the Royal Society, Dr. E. D. Adrian, who was also present.

Sir Arthur MacNalty and Dr. C. E. Lakin were reappointed as representatives on the council of the Imperial Cancer Research Fund; Dr. B. T. Parsons-Smith was reappointed as representative on the council of the Queen's Institute of District Nursing; Lord Horder was reappointed as delegate to the Annual Crema-

tion Conference to be held at Margate from July 8 to 10; and Professor A. A. Moncrieff was reappointed as representative on the Central Midwives Board under the new constitution.

Membership

The following candidates, having satisfied the Censors' Board, were elected Members of the College: H. Altman, M.B., G. C. Arneil, M.D., M. J. Bailey, M.B., C. H. Baird, M.B., S. L. Balse, M.B., P. J. Banks, M.B., J. B. Berry, L.R.C.P., D. A. Brewerton, M.D., G. H. Choa, M.B., K. M. Citron, M.D., O. Clarke, M.D., W. I. Cranston, M.B., Squadron Leader, R.A.F., J. H. Diggle, M.B., C. O. Edwards, M.B., R. W. Emanuel, B.M., J. Erulkar, M.B., R. J. Fassina, M.D., H. D. Friedberg, M.B., M. Garretts, M.B., L. Haas, M.B., P. Haden, M.B., G. V. Hall, M.B., F. Hawking, D.M., I. G. W. Hill, M.D., M. Honey, M.B., A. R. Horler, M.B., M. S. Israel, M.B., D. A. McGreal, M.B., C. J. McRae, M.B., W. E. Medd, M.B., M. O. R. Medonza, L.M.S., R. A. Melick, M.B., M. J. D. Newman, M.B., R. M. Norman, M.D., W. E. Parkes, M.D., W. M. O. Purcell, M.D., H. H. Ronn, M.B., Surgeon-Lieutenant, R.N., J. C. A. Sibley, M.D., E. S. Snell, M.B., K. L. Stuart, M.B., J. R. Sudbury, B.M., Flying Officer, R.A.F., J. L. V. Summerhayes, M.B., N. H. Wadia, M.D., D. C. Wallace, M.B., Margaret E. H. T. Warwick, B.M.

Licences

Licences to practise were conferred upon the following 149 candidates (including 33 women) who have passed the final examination in Medicine, Surgery, and Midwifery of the Conjoint Board and who have complied with the necessary by-laws: D. A. Andrews, L. G. Andrews, A. P. C. Bacon, K. D. Bagshawe, G. V. Balmforth, P. J. Barclay, N. H. Barley, D. N. Bates, D. H. Bayton, C. L. Belcourt, Ll. A. W. Bellamy, R. A. Bennett, Hilary A. Berry, Phyllis E. Billinge, E. W. G. Birch, G. W. Bisset, Joy S. Blight, Gisela Boss, R. W. Brotherwood, G. L. Brown, C. J. Buckingham, Winifred Burgess, L. J. Burns, J. D. K. Burton, A. R. Carmichael, Sylvia J. Clapp, R. H. Clark, D. L. Clarke, H. L. Clarke, Heather R. Clay, T. S. Cookson, Mary Crawford, Daphne I. L. DaCosta, R. H. Davison, J. Dennis, J. S. Dodge, D. R. Dodsley, W. A. C. Dow, Marie G. Drew, R. M. Ll. Dry, Sylvia I. Duckworth, H. P. Duke, J. Eastwood, D. W. Ebrahim, P. S. Elias, F. C. Emberton, L. L. Emery, J. Ernsting, R. S. K. Essame, Jean M. Evans, R. R. Evans, C. A. Ezike, I. R. Ferdinand, Elizabeth Fincham, R. F. Fisher, D. J. Flight, Eva A. Frommer, J. R. G. George, N. P. H. Gibbs, P. R. Gilbert, Hilary B. Gostling, D. K. Gray, D. F. Hadman, M. C. Hall, T. Hall, D. C. Harris, E. G. Haydon, N. St. J. Hennessy, L. Henry, J. H. Highman, N. A. Hiley, A. Honey, D. O. Hughes, F. C. Hurrell, J. R. F. Ingall, B. G. Jackson, Emily B. John, Thelma D. Johnson, T. G. R. Jones, Wendy Jones, R. C. Jordan, G. M. S. Keogh, Sylvia L. Kingsbury, R. M. Kirk, Daphne M. Kirkman, P. D. Lamb, J. A. Lewis, S. D. Libbert, C. A. Linsell, Betty Llewelyn, J. F. Lowe, K. R. Lown, Margaret Luing, D. McQueen, M. Malden, B. L. Mallett, C. R. A. Martin, W. A. Matheson, A. H. Maynard, B. G. Mendelsohn, T. W. Merrick, T. R. Mogila-Stankiewicz, K. S. Mooleedhar, Rosemary A. Morrell, I. G. Mowat, H. Nichol, Joyce B. Nunneley, Gillian Oliver, R. M. Oliver, C. H. Opie, Mary C. Peard, P. F. Peeks, N. T. Pollitt, E. C. V. Price, A. Rahman, D. A. Rands, J. D. Ross, N. J. W. Royston, I. Sarkany, V. Sarma, S. W. Scargill, A. S. Shamash, G. B. Skinner, J. Ll. Skinner, J. G. Slater, A. J. Smith, M. C. Solomon, A. Spellman, Margaret A. E. Stuart, H. A. J. Thomas, H. L. Thomas, Patricia M. Thompson, H. H. Thomson, O. R. Todd, Molly E. Towell, M. Tun Shwe, Barbara V. Tyman, Margaret I. Upton, Prudence Valentine, C. H. Vigar, P. O. Wakelin, Joanna M. Ward, C. H. W. Warne, G. F. Whyntie, H. J. W. Willson, R. E. Wolfendale, P. A. Woodbridge, E. G. B. Worthington, F. A. Yates.

Diplomas

Diplomas in Child Health and in Physical Medicine were conferred jointly with the Royal College of Surgeons of England to the successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of April 19 (p. 875).

Diplomas in Ophthalmology, in Anaesthetics, and in Tropical Medicine and Hygiene were conferred jointly with the Royal College of Surgeons of England as follows:

DIPLOMA IN OPHTHALMOLOGY.—L. I. Phillips and to the other successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of April 19 (p. 875).

DIPLOMA IN ANAESTHETICS.—A. E. Hocking, W. N. Wild.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—B. Devlin, A. K. Mitra, D. M. Montgomery.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending April 12 (No. 15) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	24	2	9	0	1	42	7	10	2	2
Dysentery	489	63	34	2	1	858	112	147	26	2
Encephalitis, acute	2	1	1	0		13	4	0	0	
Enteric fever: Typhoid	1	0	0	1		6	0	1	0	0
Paratyphoid	13	0	0	0		13	0	4	1	
Food-poisoning	51	6		1		142	7		1	
Infective enteritis or diarrhoea under 2 years				14	10				22	20
Measles*	5,472	210	587	250	441	22,644	1610	667	188	131
Meningococcal infection	44	2	12	1	4	46	3	14	1	2
Ophthalmia neonatorum	32	10	5	0		44	1	11	0	
Pneumonia†	680	49	291	16	1	707	37	187	18	3
Poliomyelitis, acute: Paralytic	14	2	2	1		15	2	4	0	
Non-paralytic	3	0				5	0			
Puerperal fever§	243	56	14	0		77	16	6	1	1
Scarlet fever	1,134	93	158	9	35	822	52	123	27	67
Tuberculosis: Respiratory			134	34				169	43	
Non-respiratory			25	5				28	3	
Whooping-cough	2,306	129	183	77	42	3,836	272	631	32	84

DEATHS in Great Towns	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0		0	0	*0*	0	*0*	0	0
Dysentery	1	0					0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0				*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	15	1	6	0	1	*12*		*6*	2	0
Influenza	38	3	6	0	0	*33*	4	*2*	1	2
Measles		0	1	1	2		0	*1*	0	0
Meningococcal infection		2					0	*2*		
Pneumonia	284	42		16	5	*273*	54		14	14
Poliomyelitis, acute	2	0			0	*0*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis: Respiratory	139	20	19	5	16	*160*	28	*28*	9	15
Non-respiratory		5	4	1	2		3	*1*	0	4
Whooping-cough	2	0		0	0	*11*	0	*0*	0	0
Deaths 0–1 year	248	27	34	12	13	*269*	51	*35*	12	21
Deaths (excluding stillbirths)	5,828	823	645	98	173	*5,436*	850	*632*	150	202
LIVE BIRTHS	6,887	1122	806	242	344	*6,948*	1114	*908*	249	396
STILLBIRTHS	172	15	20			*182*	23	*26*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Suspected Variola Major

A case of suspected modified smallpox was removed from a ship at Swansea on April 23 and admitted to a smallpox hospital for isolation and further investigation.

Variola Minor in Lancashire

No notification of variola minor was received for the week ending April 26, and the last reported case in the area was removed to a smallpox hospital on April 17.

Infectious Diseases

A further decrease in the incidence of infectious diseases was recorded in England and Wales during the week ending April 12. The largest falls in the number of notifications were measles 1,364, whooping-cough 698, scarlet fever 227, and dysentery 59.

The largest decreases in the number of notifications of measles were Lancashire 417, Yorkshire East Riding 177, Norfolk 174. A fall in the incidence of whooping-cough was recorded in every region of the country except the south-east counties, where a rise of 19 occurred; the largest decreases were Yorkshire West Riding 112, Lancashire 80, Kent 75. A small fall in the number of notifications of scarlet fever occurred throughout the country; the largest decreases were Lancashire 44, and Middlesex 34. The number of notifications of diphtheria was 2 more than in the preceding week. The largest variations in the returns of diphtheria were an increase of 3 in Warwickshire and a decrease of 3 in Lancashire.

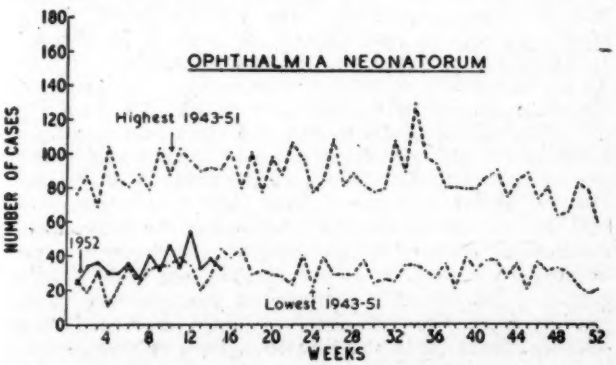
The number of notifications of paratyphoid fever was 6 more than in the previous week because of an outbreak of 8 cases in Hertfordshire, Watford, M.B.

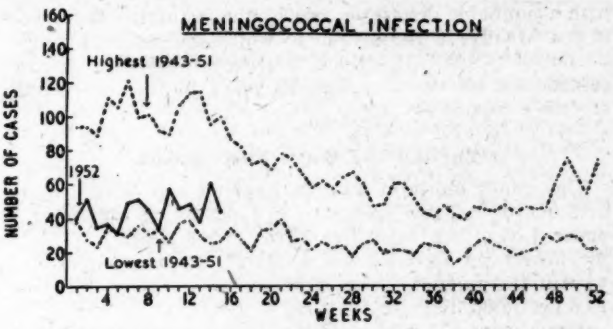
The notifications of acute poliomyelitis were 1 fewer for both paralytic and non-paralytic cases than in the preceding week. Three cases were notified in Lancashire and in Yorkshire West Riding (Leeds C.B. 2), and 2 cases in London and Warwickshire.

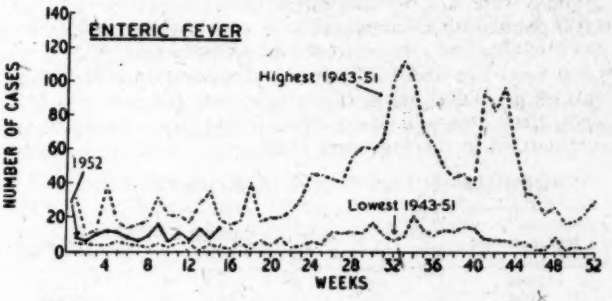
The largest centres of dysentery during the week were Lancashire 87 (Oldham C.B. 19, Whitefield U.D. 12, Manchester C.B. 11); London 63 (Poplar 14); Staffordshire 38 (Walsall C.B. 25); Yorkshire West Riding 34 (Holmfirth U.D. 22); Middlesex 34; Essex 32 (Thurrock U.D. 15); Berkshire 26 (Bradfield R.D. 12); Sussex 25 (Horsham R.D. 24); Norfolk 24 (Norwich C.B. 24); Northumberland 23.

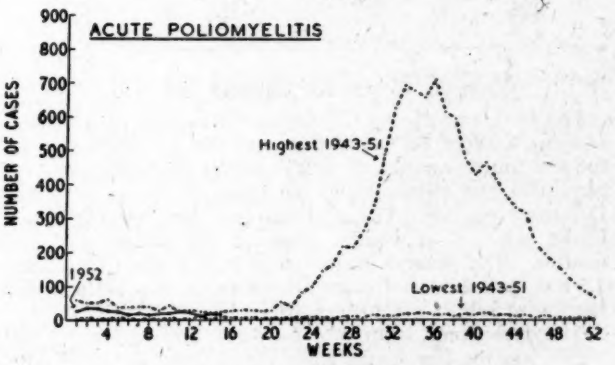
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in March was 132, compared with 114 (revised figure) in the previous month and 127 (revised figure) for March, 1951.

Cases of industrial disease reported during the month were as follows: lead poisoning 4, other poisoning 4, anthrax 5, epitheliomatous ulceration 8, chrome ulceration 25 (manufacture of bichromates 10, chrome plating 15), total 46. There were no deaths.—*Ministry of Labour Gazette*, April, 1952.

Week Ending April 19

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,043, whooping-cough 2,800, diphtheria 32, measles 6,774, acute pneumonia 820, acute poliomyelitis 23, dysentery 327, paratyphoid fever 9, and typhoid fever 2.

Tuberculosis Notifications

New regulations no longer require a medical officer of health to keep a register of tuberculosis notifications (Public Health (Tuberculosis) Regulations, 1952). But the Minister considers the M.O.H. may naturally be expected to do so (and urges that he should) in the same way as he keeps a record, for his own purposes and without any legal requirement, of notifications of other diseases. The requirement contained in the 1930 regulations for providing information of a tuberculosis patient entering or leaving a sanatorium or hospital is also omitted from the present regulations. The Minister has, however, asked hospital boards and committees to ensure that this information (as for any patient

with a notifiable disease) is sent by the institution concerned to the M.O.H. of the district to which the patient belongs. So far as the M.O.H. of the local health authority is concerned, the information finds its place in the chest clinic records available to him.

England and Wales First Quarter

The infant mortality rate in England and Wales in the first quarter of this year was 33.4 deaths of infants aged under 1 year per 1,000 live births (5,588 deaths). This is the lowest yet recorded for a March quarter, and is half what it was in 1938. The figure for the whole of 1951 was 29.6 per 1,000 live births.

There were 173,503 live births, giving a rate of 15.9 per 1,000 population as compared with 16.3 last year and 16.7 in 1950. Stillbirths numbered 4,146, giving a rate of 23.3 per 1,000 total live and stillbirths. There were 146,631 deaths, or 13.5 per 1,000 population. Last year the rate was 19.1, when there was a severe influenza epidemic. Statistics are summarized in the following Table:

First Quarter Vital Statistics in England and Wales

1st Quarter of	Infant Mortality Rate	Stillbirth Rate	Death Rate
1938	69·3	38·3	13·6
1951	38·2	23·6	19·1
1952	33·4	23·3	13·5

Quarterly Return for England and Wales

The birth rate during the December quarter of 1951 was 14.0 per 1,000 of the population, and was 0.5 below the rate for the fourth quarter of 1950. Infant mortality was 28.3 per 1,000 live births, being the same as in the preceding December quarter. The stillbirth rate, 24.1 per 1,000 total births, was 1.4 above the value of the preceding fourth quarter. The general death rate was 11.0 per 1,000, being 1.3 less than the rate for the December quarter of 1950, and the lowest rate in a fourth quarter since 1942.

The provisional birth rate for 1951 was 15.5 per 1,000, which was the lowest rate since 1941. The infant mortality rate for 1951 was 29.6 per 1,000 live births; this was the lowest rate ever recorded, being 0.4 below the rate for 1950. The general death rate was 12.5 per 1,000, being 0.9 above the rate for 1950, and the highest since 1941.

The expectation of life at birth, from an abridged life table for 1950, was 66.49 years for males and 71.22 years for females.

Medical News

Colouring Surgical Fluids.—Some time ago the Ministry of Health asked the Codex Revision Committee of the Pharmaceutical Society to suggest a standard range of colours for non-injectable fluids used in storing ampoules and syringes and in sterilizing the skin. A subcommittee set up to investigate the problem has now published its recommendations. Solutions of local analgesics for topical use should be coloured green by the addition of 1% compound solution of tartrazine, *B.P.C.*, and 1% solution of methylene blue. For a pharmaceutically suitable solution for the storage of ampoules in closed glass containers 4% chlorocresol and 1% solution of Bordeaux B, *B.P.C.*, made up in distilled water is suggested. The committee observes that it will be important to find out if this solution has a sufficiently rapid rate of kill for bacteria in the conditions under which it will be used. Surgical instruments should be stored in a solution coloured by 0.2% solution of Bordeaux B, *B.P.C.*, and hypodermic syringes in alcohol (70–75 v/v) coloured by 0.1% magenta. Of preparations containing no intrinsic colour used for skin disinfection or cleaning, aqueous solutions of cetrimide should be coloured yellow with compound solution of tartrazine *B.P.C.*—1% tartrazine in solutions containing 1% cetrimide. Industrial methylated spirit should be coloured with 0.01% magenta. Mercuric chloride solutions should be coloured with methylene blue, and 1 in 100,000 to 1 in 500,000 is suggested as a suitable range of dilution. Eosin should be used to colour solutions of mercuric iodide and oxycyanide, diluted in the same proportion. Other mercurial compounds should be coloured red or blue; eosin was precipitated in aqueous solutions of phenylmercuric acetate and nitrate, but methylene blue was found to be satisfactory for these. Fluid preparations containing phenols or chlorinated phenols should be coloured red by 1% solution of Bordeaux B. This was found suitable in all cases, while magenta was precipitated from aqueous solutions of phenol. Ether should be coloured yellow with a dye composed of 0.01% fat orange R, 0.01% of oil yellow DN, and 0.01% of waxoline yellow IS. New preparations and those not specifically mentioned here should be coloured in accordance with the recommendations, and if no recommendation applies they should wherever possible be coloured yellow. The committee stresses that it is dangerous to rely solely on coloured solutions for identification purposes and urges that containers should as far as possible be labelled clearly.

Heberden Society.—The Heberden Round was conducted by the president of the society, Sir Henry Cohen, at the Royal Infirmary, Liverpool, on April 18, when he showed a variety of cases of the diffuse collagen diseases which had been under treatment with cortisone and A.C.T.H. Four cases of disseminated lupus erythematosus, each exhibiting differing grades of skin and visceral involvement varying from a dermatitis with the smallest constitutional change to a slight rash with multiple involvement of serous membranes, had shown general improvement with A.C.T.H., but in at least one case the histology remained unchanged. A child with dermatomyositis was being maintained on a small amount of A.C.T.H. given every few days: attempts to substitute cortisone to avoid injections resulted in a rapid relapse. An advanced case of scleroderma had failed to respond to intravenous A.C.T.H. A woman with Sjögren's syndrome, including swollen and painful parotid glands, granulopenia, arthritis, and hepatitis, showed evidence of improved hepatic function. Other cases were also shown. Sir Henry Cohen entertained the members of the society to dinner at the Staff House of the University of Liverpool.

Association of British Pharmaceutical Industry.—The annual dinner was held at the Savoy Hotel on April 23. Proposing the toast to the industry, Dr. Ffrangcon Roberts referred to the spectre of nationalization and wondered whether the eventual prospect was one of alternate nationalization and denationalization with successive governments. But, whatever the future might bring, he was confident that the industry would surmount its difficulties with the help of those great qualities through which it had already made valuable contributions to national prosperity. The president of the association, Mr. J. C. Hanbury, after congratulating Dr. Roberts on his recent book, *The Cost of Health*, which he described as a penetrating analysis of one of the major social problems of the day, spoke of the medical difficulties inevitably associated with an ageing population. The very high cost of prolonging the life of aged people was perhaps insufficiently appreciated by governments. There was a tendency to make the pharmaceutical industry the scapegoat for extravagance for which it was in no way responsible. The health of the guests was proposed by Mr. J. F. Boucher: two Scotsmen replied with the characteristic brilliance expected of the Glasgow and Edinburgh schools. Mr. Walter Elliot, apologizing for a rather hurried visit from Westminster, said that the astonishing new addiction of the public to the excellent products of the pharmaceutical industry was preoccupying the attention of M.P.s. Professor D. M. Dunlop remarked that scientific therapeutics was only just getting into its stride: no one could say what the speed of its advance would be in the next 50 years—"We might even

be able to prevent the common cold." The universities, he thought, would fight a losing battle in competition with research backed by the pharmaceutical industry, of whose achievements they could be very proud. On the other hand, there was perhaps a less altruistic side to the industry's work, encouraged no doubt by the fact that a desire to take medicines was the chief thing which differentiated man from animals.

Isonicotinyl Hydrazide in Devon.—The Devon and Exeter Medico-Chirurgical Society had a meeting at the Hawkmoor Chest Hospital, Bovey Tracey, on April 17, when Dr. Midgley described experience with *iso*nicotinyl hydrazide in four tuberculosis cases, the usual dosage being 100 mg. four times a day.

A woman aged 23 had been in hospital for 2½ years, was steadily going downhill, and running a temperature of 101° F. (38.3° C.) every night, with a positive sputum count of 10 per field. With the drug her temperature rapidly settled to normal, the sputum count at the end of a week was 5 per field, later dropped to 1 per field, and finally after two months to 1 in 50 fields, and there was a material improvement in the general condition. In another case with active lesions in the lungs and a large psoas abscess the sputum became negative, the fever abated, and the pus aspirated from the abscess became thin and clear instead of thick and purulent. A child who had not responded to streptomycin showed a marked improvement, and another patient showed some improvement though not quite such a dramatic effect on the temperature.

Glasgow Royal Cancer Hospital Changes Name.—By gracious permission of the Queen the Glasgow Royal Cancer Hospital and Glasgow and West of Scotland Radium Institute will now be called the Royal Beatson Memorial Hospital, in honour of the late Sir George Beatson, who more than anyone else was responsible for the establishment of the hospital and its research department. There will be no change in policy or staff.

New Midwives Board.—The Central Midwives Board has been re-formed, and medical men appointed as members for three years from April 1 are: J. A. Scott, J. G. Thwaites, and A. L. Walker (chairman) by the Ministry of Health; Professor A. Moncrieff (vice-chairman) by the Royal College of Physicians; Professor A. M. Claye by the Royal College of Surgeons; V. Lack by the Royal College of Obstetricians and Gynaecologists; J. M. Gibson by the Society of Medical Officers of Health; A. Elliott by the County Councils Association; and Professor F. E. Tylecote by the Association of Municipal Corporations.

Prizes for Medical Films.—On April 4 at Paris the prizes were awarded for the best 16-mm. films in the first competition organized by *La Presse Médicale* (see *British Medical Journal*, February 16, p. 393). There were several British entries, including "Preparation of the Frog's Sciatic Nerve," by Bligh and Rashbass, which won one of the four prizes of 10,000 francs. First prize (50,000 francs) went to Drs. Pierre-Marion, Gard, Grégoire, Termet, and Deleuze, all of Lyons, for "La Réanimation du Cœur"; two second prizes (25,000 francs each) to "La Bronchocinématographie," by Dr. Fourestier and MM. Vulmière and Gladu, and "La Vie des Plus Petits Prématurés" by Drs. Rossier and Michelin, all of Paris. Judgment was based on both teaching and cinematic quality, and many of the films were in colour. There were 26 French doctors, and nine from England, Belgium, Italy, and South Africa, who submitted one or more entries.

Centenary of Cajal.—Santiago Ramón y Cajal, who was born 100 years ago on May 1, was the father of Spanish science. For over 50 years he made important contributions to knowledge of the anatomy of the nervous system, though his work was often neglected because it was published in Spanish. One of his greatest achievements lay in stimulating scientific education in his own country. The son of a struggling Aragonese doctor, he learnt various trades before his father began to teach him osteology. He studied medicine at Saragossa, became licentiate in 1873, and graduated M.D. four years later. He became professor of anatomy at Barcelona in 1887, and here began his long study of neuro-histology, continuing his work later at Madrid. By 1894 he had written a manual of pathological histology and published a great many papers. In that year he gave the Croonian Lectures in London, and formed a lasting friendship with Sherrington. His great work, *Textura del Sistemo Nervioso del Hombre y Vertebrados*, was written soon after his visit to London. In 1934 he was elected a foreign corresponding member of the B.M.A.

Dr. F. M. R. Walshe is to give the Thayer Lectures at the Johns Hopkins Hospital, Baltimore, in May, and to be the guest speaker at the annual meeting of the Canadian Neurological Society at Banff in June.

Dame Hilda Lloyd.—A bronze bust by Epstein of Dame Hilda Lloyd was unveiled in the entrance hall of the medical school at Birmingham University on April 21.

Drs. S. Barron, W. E. Chiesman, S. W. Fisher, A. Massey, R. H. Parry, and **H. J. Rae** have been appointed Honorary Physicians to the Queen till June 30, 1953.

Emergency Bed Service: Applications and Admissions.—During the seven days ending April 28 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 970, of whom 88.81% were admitted.

COMING EVENTS

Glasgow Medical Exhibition.—The exhibition is to be held this year at St. Andrew's Hall, Glasgow, from May 26 to 30 inclusive. Mr. W. W. Galbraith will open the exhibition at 11.30 on May 26. Attendance is confined to members of the medical profession, and exhibits will include many of the latest developments in medical products and a wide range of surgical and other professional apparatus. There will be performances each day of films of professional interest.

Housing the Ageing.—This is the topic for the University of Michigan Fifth Annual Conference on Ageing to be held in Ann Arbor, Michigan, July 24–26. The three-day conference will consider the housing needs of healthy, chronically ill, confused, and disabled older people living in urban and rural areas. Among the topics to be discussed are types of housing and living arrangements; architectural designs and costs; hygiene and safety standards; social and economic aspects of housing; and auxiliary services. The conference is designed to serve as a forum for interchanging information and for getting action on the difficult problem of financing housing for the ageing. Conference registration materials may be obtained by writing to Dr. Wilma Donahue, Institute for Human Adjustment, Room 1510, Rackham Building, Ann Arbor, Michigan, U.S.A.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, May 2

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—3.45 p.m., *"Bone Dystrophies,"* Erasmus Wilson Demonstration by Mr. L. W. Proger.

Monday, May 5

EDINBURGH UNIVERSITY.—At Surgery Lecture Theatre, University New Buildings, Teviot Place, 5 p.m., *"Studies in Surgical Metabolism—(1) The Metabolic Response to Surgery,"* by Professor F. D. Moore (Harvard). (See also May 6 and 7.)

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., *"Development at the Cellular Level—Self-reproducing Particle in the Development of Ciliates,"* special university lecture by Dr. A. Lwoff (Paris). (See also May 6 and 8.)

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., *"The Care and Treatment of the Myopic Patient,"* by Dr. T. H. Whittington.

UNIVERSITY COLLEGE, LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 4.45 p.m., *"Chemical Structure, Interaction, and Fractionation of Proteins,"* public lecture by Professor J. T. Edsall (Harvard).

Tuesday, May 6

CAMBRIDGE UNIVERSITY.—At Anatomy School, 5 p.m., "*The Fabric of Surgery*," Linacre Lecture by Sir James Learmonth.

EDINBURGH UNIVERSITY.—At Surgery Lecture Theatre, University New Buildings, Teviot Place, 5 p.m., "*Studies in Surgical Metabolism—(2) Surgical Metabolism and the Endocrine Glands*," by Professor F. D. Moore (Harvard). (See also May 5 and 7.)

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., "*Development at the Cellular Level—Life Cycle of Bacteriophage in Lysogenic Bacteria*," special university lecture by Dr. A. Lwoff (Paris). (See also May 5 and 8.)

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—5 p.m., "*Reason and Unreason in Psychological Medicine*," Croonian Lecture by Dr. E. B. Strauss. (See also May 8.)

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5 p.m., "*Genetics in Ophthalmology*," by Professor Arnold Sorsby.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, London, W.—5 p.m., "*Pathology at the Crossroads*," by Professor G. R. Cameron, F.R.S.

Wednesday, May 7

CAMBRIDGE MEDICAL SOCIETY.—At University Arms Hotel, 7.30 for 8 p.m., dinner.

CAMBRIDGE UNIVERSITY.—At Senate House, Cambridge, 5 p.m., "*The Contribution of Medicine to our Idea of the Mind*," Rede Lecture by Sir Russell Brain, P.R.C.P.

EDINBURGH UNIVERSITY.—At Surgery Lecture Theatre, University New Buildings, Teviot Place, 5 p.m., "*Studies in Surgical Metabolism—(3) The Study of Body Composition by Isotope Dilution*," by Professor F. D. Moore (Harvard). (See also May 5 and 6.)

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—8 p.m., films of ophthalmic operations.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., "*Hospital Infections*," by Dr. J. O. Oliver.

MANCHESTER MEDICAL SOCIETY.—At Physiology Theatre, Manchester University, 4.15 p.m., annual meeting. "*Twins*," by Dame Hilda Lloyd.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—5.30 p.m., "*Ptosis*," by Mr. L. H. Savin.

ROYAL MICROSCOPICAL SOCIETY: BIOLOGICAL SECTION.—At Tavistock House (South), Tavistock Square, London, W.C., 6 p.m., "*Rhythmic Pulsatile Activity in Cells from the Central Nervous System*," by Professor C. M. Pomerat (University of Texas).

Thursday, May 8

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., 8 p.m., "*Individual and Social Psychology*," by Lewis Way. A discussion will follow.

EDINBURGH UNIVERSITY, University New Buildings, Teviot Place.—At Anatomy Theatre, 5 p.m., "*Some Problems Involved in the Treatment of Portal Hypertension*," Honyman Gillespie Lecture by Mr. A. I. S. MacPherson.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., "*X-ray Technique*," by Dr. C. W. McKenny.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Maternity Hospital, Goldhawk Road, Hammersmith, W., 11 a.m., "*Breast-feeding*," Guest Lecture by Dr. H. K. Waller.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—5 p.m., "*Diagnosing Personality in Primates*," public lecture by Professor D. O. Hebb (Montreal).

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., 5.30 p.m., "*Development at the Cellular Level—Induced Development of Viruses and of Non-infectious Particles*," special university lecture by Dr. A. Lwoff (Paris). (See also May 5 and 6.)

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, London, S.W.—5 p.m., "*Reason and Unreason in Psychological Medicine*," Croonian Lecture by Dr. E. B. Strauss. (See also May 6.)

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—3.45 p.m., "*Pectoral Girdle*," Arnott Demonstration by Professor R. J. Last; 5 p.m., "*The Surgery of Accidents and its Social Significance*," Joseph Henry Lecture by Mr. William Gissane.

ST. ANDREWS UNIVERSITY.—At Materia Medica Department, Medical School, Small's Wynd, Dundee, 5 p.m., "*Benign and Malignant Hypertension*," by Professor G. W. Pickering.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—5 p.m., lecture-demonstration in psychiatry by Sir Paul Mallinson.

UNIVERSITY COLLEGE, LONDON.—At Anatomy Theatre, Gower Street, W.C., 5 p.m., "*Contributions of Psychology to Social Problems*," Hobhouse Memorial Lecture by Sir Cyril Burt, D.Sc.

WEST END HOSPITAL FOR NERVOUS DISEASES.—At 48, Cosway Street, Marylebone Road, London, N.W., 5.30 p.m., "'*Functional*' *or* '*Organic*' *Differential Diagnosis*," by Dr. Colin Edwards.

Friday, May 9

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—5.30 p.m., "*Eczema*," clinical demonstration by Dr. J. E. M. Wigley.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—4.30 p.m., "*Plastic Operations and Orbital Surgery*," by Mr. A. J. Cameron.

Saturday, May 10

●ROYAL DENTAL HOSPITAL OF LONDON: SCHOOL OF DENTAL SURGERY, 32, Leicester Square, W.C., 2 p.m., annual clinical "At Home."

APPOINTMENTS

FERGUSON, T. B., M.B., Ch.B., D.P.H., Medical Officer, British Railways (Scottish Region, Glasgow).

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Whole-time Consultant Child Psychiatrist, with duties mainly at Alder Hey Children's Hospital, Liverpool*, Philip Pinkerton, M.B., Ch.B., D.P.M. *Whole-time Consultant Physician-Superintendent, Sefton General Hospital, Liverpool*, C. S. McKendrick, M.B., B.Chir., M.R.C.P. *Consultant Physician to St. Helens and District Hospital Management Committee Group*, N. Bennett Jones, M.B., Ch.B., M.R.C.P. *Whole-time Consultant Radiotherapist to Liverpool Radium Institute*, W. Kulke, M.B., Ch.B., M.Rad., D.M.R.T. *Consultant Obstetrician and Gynaecologist to Walton Hospital*, S. J. Barr, M.B., B.Ch., F.R.C.S.Ed., M.R.C.O.G.

MANCHESTER REGIONAL HOSPITAL BOARD.—*Assistant Pathologist to Group Laboratory of Withington Hospital, with main duties at Christie Hospital and Holt Radium Institute, Manchester*, J. A. Shrigley, M.B., Ch.B. *Assistant Radiologist, Wigan and Leigh Hospital Centre*, G. H. Waddington, M.R.C.S., L.R.C.P., D.M.R.D.

PARRY, T. E., M.B., Ch.B., M.R.C.P., Whole-time Consultant Pathologist, Llandough Hospital (United Cardiff Hospitals).

PERROTT, Ethel Anne, M.D., D.P.H., Medical Officer of Health, Millom Rural District Council, and Assistant County Medical Officer of Health, Cumberland.

SOUTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Whole-time Consultant Pathologist, Woking and Chertsey Group of Hospitals*, C. F. Ross, M.D. *Whole-time Deputy Physician-Superintendent and Consultant Psychiatrist, Netherne Hospital*, H. E. S. Marshall, M.B., B.Chir., D.P.M. *Whole-time Assistant Psychiatrist (S.H.M.O.), St. Ebba's Hospital*, G. H. A. Chamberlain, M.D., M.R.C.P.I., D.P.M. *Whole-time Assistant Psychiatrist (S.H.M.O.), E.E.G. Department, St. James' Hospital, Portsmouth*, E. V. Mellor, M.D. *Consultant Pathologist, Southampton Group of Hospitals*, S. C. Dobson, B.M., B.Ch. *Whole-time Consultant Pathologist, Croydon Group of Hospitals*, H. T. Stewart, M.D., D.T.M.&H. *Whole-time Assistant Pathologist (S.H.M.O.). Guildford Group of Hospitals*, A. Lawrence, M.B., Ch.B. *Psychiatric Registrar, St. James' Hospital, Portsmouth*, C. Donovan, M.B., B.Ch. *Psychiatric Registrar, Cane Hill Hospital*, Carmel P. Dooley, L.R.C.P.&S.I. *Radiological Registrar, Royal South Hants Hospital*, Mrs. Margaret P. Sheridan, M.B., B.Ch., D.M.R.D. *Radiological Registrar, St. Peter's Hospital, Chertsey*, A. T. Broadbridge, M.R.C.S., L.R.C.P., D.M.R.D. (Part I). *Senior Medical Registrar, St. Peter's Hospital, Chertsey*, A. P. C. Bacon, M.B., B.Chir., M.R.C.P. *Medical Registrar, Dorset County Hospital*, R. E. Gruchy, M.B., B.Chir. *Medical Registrars, St. Stephen's Hospital, Chelsea*, P. R. Fleming, M.D., M.R.C.P., and Audrey S. Willis, M.B., B.Chir.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cooper.—On April 23, 1952, at Parklands Drive, Fulwood, Preston, Lancs, to Hazel, wife of Dr. W. A. Bruce Cooper, a daughter.

Llewellyn.—On April 15 1952, at the Royal Infirmary, Falkirk, to Dr. Anne McLachlan (formerly Haddow), wife of Dr. Oliver Llewellyn, M.C., a daughter.

MARRIAGES

Gribble—Watkins.—On April 19, 1952, at Dulwich, London, S.E., Michael de Gruchy Gribble, B.M., B.Ch., to Patricia Mary Watkins.

DEATHS

Barnett.—On April 24, 1952, at Bath, Henry Norman Barnett, F.R.C.S.Ed., Lieutenant-Colonel, R.A.M.C., retired.

Carr.—On April 24, 1952, at 1,007, High Road, Whetstone, London, N., Richard Joseph Carr, M.B. B.Ch.

Forbes.—On April 22, 1952, at Beech House, High Street, Knaresborough, Yorks, William John Forbes, M.B., B.Ch., aged 81.

Horner.—On April 23, 1952, William Ernest Leetham Horner, M.D., of Ravenswood, Hassocks, Sussex, formerly of Wolstanton, aged 80.

Ives.—On April 21, 1952, at 25, Malmains Way, Beckenham, Kent, William Frank Hague Ives, L.R.C.P.&S.Ed., L.R.F.P.S., aged 72.

Jolliffe.—On April 25, 1952, William Edwin Jolliffe, L.R.C.P.&S.I. & L.M., of Harleston, Norfolk, formerly of Southampton, aged 84.

Lace.—On April 22, 1952, Frederick Lace, T.D., F.R.C.S., of 5, Gay Street, Bath, aged 88.

McGibbon.—On April 21, 1952, at Edinburgh, John Paton McGibbon, M.D., F.R.C.P.Ed., D.P.H., D.R.

Marshall.—On April 23, 1952, at Hilden, Bideford, Devon, Arthur Thomson Marshall, M.B., B.S.

Parker.—On April 16, 1952, at Grantham Hospital, Alfred Parker, L.R.C.P.&S.Ed., L.R.F.P.S., of The Mount, Corby Glen, Grantham, Lincs.

Roberts.—On April 25, 1952, at Dragonfield, 14, Hailsham Road, West Worthing, Sussex, Frederic Emilius Roberts, D.S.O., O.B.E., M.R.C.S., L.R.C.P., D.P.H., Lieutenant-Colonel, R.A.M.C., retired, aged 73.

Taylor.—On April 24, 1952, at The Laurels, Hailsham, Sussex, Thomas Sigston Taylor, B.Chir.

Thompson.—On April 18, 1952, at his home, Oughtibridge House, Oughtibridge, near Sheffield, Yorks, James Alexander Richard Thompson, M.D., D.P.H., aged 76.

White.—On April 23, 1952, at The Firs, Prestwood, Bucks, Gilbert Benjamin Mower White, M.B., F.R.C.S., aged 86.

Woodruff.—On April 23, 1952, Charles Reynolds Woodruff, M.B.E., M.R.C.S., L.R.C.P., L.D.S., of 1, Bentinck Street, London, W.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Antibiotics for Underweight Infants

Q.—*"Aureomycin" and chloramphenicol have been used to promote growth in poultry and animals. Are these antibiotics likely to be useful in the treatment of retarded growth in children who show no obvious endocrine disorder?*

A.—There have been no reports of the effect of chloramphenicol on growth, but aureomycin has been found to make a marked difference in the weight gain of infants suffering from fibrocystic disease of the pancreas. It has also been used for premature babies, and in a small series recently reported the treated infants gained weight more rapidly than did the controls, perhaps because they were protected by the aureomycin from the infections which attacked a number of the controls.

These antibiotics are not without danger, especially in the youngest age groups, because of their interference with normal vitamin synthesis in the gut and because of their effect on the mouth. Stomatitis and thrush have repeatedly occurred, and the possibility of the development of a generalized moniliasis must also be borne in mind. Their use in the treatment of retarded growth in children is not advisable unless, perhaps, the growth retardation is clearly associated with chronic or repeated infection.

Fate of Milk after Arrested Lactation

Q.—*It occasionally becomes necessary to prevent lactation proceeding normally. In the case of breasts secreting normally at, for instance, the fifth day of the puerperium, I assume that the ampullae and main tubules are full of milk, and even if this is rapidly removed before bandaging there will be, for a time, a substantial residuum. What happens to this milk, and what is the detailed mechanism of removal?*

A.—There is not very much clear-cut information on the subject, as experimental work is so scanty. We do know, however, that a sufficient increase of pressure inside the mammary gland will stop secretion. If a lactating mammal is not milked, then the pressure inside the gland steadily rises as more and more milk is secreted. In the cow, when the additional pressure, above that normally existing when the udder is just full, reaches about 25 mm. Hg (which may be, say, 24 hours after cessation of milking) secretion stops and reabsorption of milk begins. After another 48 hours or so the pressure has fallen and the composition of the remaining milk has changed considerably. It is now moving in composition in the direction of blood plasma. The percentage both of lactose and of fat falls fairly quickly, the sodium chloride increases, the *p*H tends to move from the normal milk *p*H (of 6.4 to 6.6) towards 7.3. Then, after an increase in total protein, the casein percentage falls, and albumin and globulin appear to come in from the blood. All this time the amount of fluid has diminished, and continues to diminish, as it is reabsorbed from all parts of the gland, including the collecting sinuses. All secretion has apparently stopped at the peak of the pressure period and has not begun again. If the cow is milked before much milk has been reabsorbed, then the process is partially reversible and the cow can usually be brought back into some, if not full, production again. If the animal is not milked, and sometimes if, with milk residues still in the gland, attempts are made to milk her, the drying-up process will continue.

The writer cannot give as much information about the same process in the breast; doubtless there will be a similar course of events. Something is now known about the detailed biochemistry of milk secretion, but not very much, apart from what has been summarized above, about the biochemistry of reabsorption. Presumably many of the chemical reactions involved in milk secretion by the alveolar cells are balanced ones that are capable of reversal, but it appears that this process of reversal also destroys, in a fairly short time, the secreting cells. Whether udder secretion stops suddenly, or whether it slowly ceases in the normal way, these cells appear to be completely renewed before the next lactation. Thus, in the cow, a "quarter" damaged by streptococcal or staphylococcal mastitis may be freed from pathogenic organisms by antibiotic therapy, but will in most cases not recover its lactational ability in that lactation. In the subsequent lactation, however, it usually will give as much milk as the corresponding quarter which was *not* infected.

Sweethearts

Q.—*What are the causes of the white spots which sometimes appear on the fingernails? Have anxiety or minute traumata during manicure anything to do with their appearance?*

A.—Abnormalities of the growth of the nails form a somewhat neglected branch of dermatology, partly because their histological study presents considerable technical difficulties. These white spots on the nails (leukonychia, "milk spots," "sweethearts") are variously supposed to be due to persistent keratohyalin granules or to the presence of minute bubbles of air in the substance of the nail.

Sometimes the spots occur as an inborn abnormality, and in these cases may be familial; it is usually then that the whole of all the nails is thus affected. Acquired patchy leukonychia has been described as a consequence of arsenical and other intoxications. In these cases, too, it is usual for all the nails to be symmetrically affected. It is said that leukonychia may result from attacks of Raynaud's disease. However, far the commonest form of leukonychia is the occasional appearance in one nail at a time of occasional dead-white or fluffy-white spots a few millimetres across. They are very common in children but not so often seen in adults. Nothing certain is known of their cause. If they were due to some systemic disturbance of physical health or to anxiety one would expect them to appear simultaneously in all the nails, which they rarely do. If they were due to slight manicure injuries one would expect them to be a more obvious consequence of injuries, and their predominance in children makes this hypothesis unlikely. Both of these theories of causation are often mooted and are difficult to disprove, but the evidence in favour of them is scanty. T. L. Tyson (*J. invest. Derm.*, 1950, **14**, 323) has reported improvement of the nails in various other dystrophies following the consumption of half an ounce (15 g.) of gelatin per day for several months. This simple and harmless treatment would be worth trying.

Quaternary Ammonium Antiseptics

Q.—*What are the clinical advantages attaching to antiseptics of the quaternary ammonium type over the older forms such as chlor-xylenols, lysols, etc.?*

A.—Their advantages are (1) very low tissue toxicity, (2) cleansing action (of particular value in immediate wound treatment), and (3) odourlessness. On the other hand, their capacity to kill bacteria is inferior to that of other antiseptics which may be used for the same purposes. They have a comparatively weak action on Gram-negative species: if a solution of cetrimide is placed in an unsterilized bottle with a bark cork, *Ps. pyocyanea*, apparently derived from the cork, may be found in the solution itself (see E. J. L. Lowbury, *Brit. J. industr. Med.*, 1951, **8**, 22).

Vitamin Supplements in Tuberculosis

Q.—*What is the scientific basis of the traditional administration of supplements of vitamins A and D in tuberculosis? Are there dangers in this?*

A.—It is not necessary to give supplements of vitamins A or D to patients with pulmonary tuberculosis. The tradition is based on a pious hope and a craving for the magical rather than on science. Any person on a normal diet is known to receive adequate supplies of these vitamins. The patient with active tuberculosis should obtain the extra rations to which he is entitled, together with 1½ to 2 pints (0.8 to 1.1 litres) of milk daily. These will be more than ample to ensure that he does not suffer from vitamin deficiency.

Calciferol in Tuberculosis

Q.—*How does calciferol facilitate streptomycin and P.A.S. therapy in tuberculosis, and is its use recommended?*

A.—Calciferol, when used in the treatment of lupus vulgaris, causes a preliminary phase of congestion and exudation in the lesions, followed by contraction and healing. There is also some evidence that calciferol may produce a focal exudative reaction around the lesions of pulmonary tuberculosis and thus cause them to spread. It was thought that, by combining calciferol with streptomycin and *para*-aminosalicylic acid (P.A.S.), the vascular and exudative response to the calciferol might bring the antibiotic more effectively to the site of the lesion, while at the same time the streptomycin would prevent any dangerous effect of the calciferol. The method has been tried in only a very few cases, and, although the results are said to have been encouraging, it should certainly not be brought into general use until further trials have been made.

First Successful Pneumonectomy

Q.—*About the time of the last operation on King George VI it was stated in more than one newspaper that Sir William Macewen had performed pneumonectomy at the Western Infirmary, Glasgow, in 1895 on a man with a tuberculous cavity. Is there any record of this, and is it the first recorded case of a successful pneumonectomy?*

A.—It is quite true that Macewen performed the first successful pneumonectomy in 1895. The circumstances of the operation and the subsequent fate of the patient are vividly described in A. K. Bowman's biography of Macewen,[1] from which the details given below are taken. The operation was recorded in detail by Macewen himself in his Cavendish Lecture of 1906.[2]

The patient, R. W., was in the wards of Sir William Tennant Gairdner in the Western Infirmary, and was suffering from an empyema superimposed upon bilateral pulmonary tuberculosis. He was said to be moribund by Gairdner, who felt that surgical care might ease his last few days, and therefore asked Macewen to accept him in his wards. On April 24, under light chloroform anaesthesia, Macewen made an incision over the seventh and eighth ribs on the left side and resected two inches of each exposed rib. The periosteum and pleura were perforated and 160 oz. of pus evacuated. This was found to be loaded with tubercle bacilli, staphylococci, and streptococci. The lung tissue was densely adherent to the chest wall and was methodically excised. At the end of the operation the cavity was washed out, packed with gauze, and drained. The patient reacted well, and soon experienced great symptomatic relief.

A month later Macewen performed thoracoplasty in order to explore the chest cavity thoroughly and to clear any shreds of lung tissue still remaining. It was found that, except for some shreds of tissue adherent to the chest wall and a small fragment at the apex, the lung had been completely removed at the first operation. The patient appears to have made an uninterrupted recovery, and, so far as it was possible to judge, the disease in the right lung became quiescent. The patient subsequently resumed his occupation. He was demonstrated to and examined by a number of physicians in June, 1906, and again in 1913 and 1920. Macewen himself relates a dramatic encounter with the man one foggy November evening about the year 1914.

"At a street corner, in the circle of murky light cast down by a fog-enshrouded lamp, I observed a little group of people. Curious, and anxious to learn what brought the people out of doors on such a night, I moved closer. A meeting was taking place. It was a gathering of that admirable body which calls itself . . . the Salvation Army. And in the middle of the circle stood a man, and he was making an address, unconscious for the moment of the frost and fog and snow. I glanced at him, and I recognized my patient of many years ago—the man with but one lung."

Dr. Bowman records that when he was about to read the proofs of the chapter of his book dealing with R. W. he was astounded to learn from a surgeon to the Royal Infirmary that R. W. was not only alive but still in excellent health at about 70 years of age and 42 years after Macewen's operation. As recently as the end of 1940 he underwent an operation for the radical cure of hernia.

REFERENCES

1 *The Life and Teaching of Sir William Macewen*, London, 1942.
2 *British Medical Journal*, 1906, 2, 1.

Over-sexed Girls

Q.—*Having found stilboestrol therapy effective in causing the disappearance of the hypersexual state in homosexual males, I would like to know if there is any drug which can be used to diminish the libido of over-sexed girls of delinquent pattern?*

A.—The writer knows of no specific drug or hormone which can diminish the libido of "over-sexed girls." In males stilboestrol inhibits the secretion of the pituitary gonadotrophic hormone, and as a result the testes lose their normal pituitary stimulus and may even atrophy; thus the secretion of testicular testosterone is diminished or abolished; and as testosterone plays an important part in libido and potency there is a resulting diminution, or disappearance, of these. In the case of the female, testosterone would diminish the secretion of endogenous oestrogens by suppressing pituitary gonadotrophic secretion, but in addition it has important direct actions, particularly on the clitoris, hypertrophy of which, in some females, increases libido and eroticism. Biochemical work is being carried out to find hormones or allied substances which suppress pituitary activity without being appreciably androgenic or oestrogenic. The giving of stilboestrol or oestrogens to females is unlikely to diminish libido and might increase it.

The First Barbiturate

Q.—*Who first introduced the barbiturates into medicine, and when? Which of them was first used?*

A.—E. Fischer and J. von Mering in 1903 (see *Fifty Years of Medicine*, obtainable for 15s., including postage, from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1). The first barbiturate to be used in medicine was barbitone (diethylbarbituric acid).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London*. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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